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THE CYTOLOGY OF GLANDULAR SECRETION

BY ROBERT H. BOWEN

Department of Zoölogy, Columbia University

(*Editorial Note:* While this paper was passing through the press Dr. Robert Hall Bowen died, at the age of thirty-seven, after a very brief illness. The loss to biology from the passing of this brilliant young investigator, just at the start of a career of extraordinary promise, is irreparable.)

INTRODUCTION

Pour nous, histologistes ou histophysiologistes, la sécrétion consiste essentiellement dans l'élaboration au sein du protoplasma des cellules d'un matériel spécial qui caractérisera le produit de sécrétion de la glande.

(Ranvier, 1887.)

IT IS a striking characteristic of metazoan cells that at some stage in their history structures of various kinds are built up in the cytoplasm. This phenomenon—differentiation— results in making cells histologically diverse. Thus in certain cells muscle-fibrils appear, in others neurofibrils and Nissl substance, yolk, and so on. Of these differentiation-products some are relatively permanent, as in muscle or nerve cells, and become an integral part of the cell containing them. In other cases, however, the products of differentiation are transitory and may disappear again into the cytoplasm from which they seemed to be evoked—as in case of yolk in a developing egg; but more commonly such products are formed only to be eliminated from the cell like the zymogen granules of the pancreas. Broadly speaking, therefore, the problem of "secretion" is not confined to the evacuation of a fluid, as usually conceived by the physiologist, but includes all that large group of phenomena in which materials of many kinds are elaborated in the cytoplasm only to be returned to the cell-system, or else extruded as a part of some secretion. The problem of glandular secretion thus shapes itself for the cytologist in terms decidedly different from those to which the physiologist is accustomed. "Secretion," for the cytologist, has nothing to do with mere extrusion from the cell, but refers rather to those recondite processes by which the cell elaborates the specific elements of the extruded material. This contradiction in terms was pointed out by Ranvier as long ago as 1887, and is doubtless traceable to the fact that the flow of liquid from a gland was studied long before even the cellular basis of living matter was suspected. Quoting Ranvier ('87, p. 13):

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Par exemple, si l'on excite par un courant d'induction interrompu le nerf sécrétoire d'une glande muqueuse, on voit l'excitation du neuf suivie d'une abondante sécrétion. C'est l'acte sécrétoire des physiologistes. Pour eux, la sécrétion d'une glande muqueuse ne consiste pas dans l'élaboration du mucigène au sein des cellules, mais dans la formation et l'issue du mucus. Or, si l'on analyse le phénomène, si, au lieu de prendre le résultat entier du travail glandulaire, on considère le phénomène histologique, on est porté à penser, au contraire, que la sécrétion consiste dans l'élaboration du mucigène et que ce que les physiologistes appellent sécrétion n'est qu'un phénomène d'excrétion.

Unfortunately, the term "excretion" has come to have a rather definite meaning, quite different from that suggested by Ranvier, and J. Müller's distinction between an "excretion" and a "secretion" is still largely followed. Thus the essence of a secretory process, namely, the origin of the substances specific to glandular products, has been neglected by the physiologist, and he has felt no need even to name a process of which he takes practically no cognizance. But it is exactly this aspect of the problem which interests the cytologist, for whom even the "excretions" of physiological terminology may in many cases belong to his broader category of "secretions."

Whether there is any real significance in these distinctions may perhaps best be left undecided, but for practical purposes we must come to some terms with these differences in current usage. In this review I shall accordingly follow Ranvier, and restrict the term "secretion" to the process of intracellular synthesis. Similarly the process of extrusion, or the emptying of a gland-cell, will be called "excretion." It may be noted that these difficulties in terminology led Matthews ('99) to suggest that "secretion" be retained in its present physiological sense, and that the synthetic process within the cell be termed "hylogenesis." I am inclined to believe that some such solution of the difficulty may eventually prove most feasible.

The present review proposes to deal only with the secretory phenomena in so-called glandular cells. Even in so limited a category of cells, it is a moot point as to whether secretion is invariably an expression of one essential process, or whether in different types of glands, different morphological origins are to be expected. It is my own feeling that the phenomena of glandular secretion are based on some plan common in its essentials to all gland-cells. The more we learn about the cell, the more evident does it become that a given life-process, at first described with many patterns, is gradually resolved into numberless variations of a single basic procedure. With expanding horizons, the unity of a particular cell-activity seems ever more significant. It is, therefore, safe to suggest that experience should caution us against the easy acceptance of accounts of cell-mechanisms for secretion, which are diametrically opposed. The fact that two cells produce radically different secretions scarcely warrants the assumption that the mode of production can also be fundamentally different in the two cases. Cytological interpretations of particular secretory cells, which take no account of the known elements of both cytoplasm and nucleus, and neglect to seek for some wider correlation with the varied aspects of secretory phenomena in general, forfeit, it seems to me, any claim to serious consideration at the present time.

The cytological problems presented by secretory activity have for many years offered an attractive field for investigation, but they have in recent years assumed an added interest in the light of suggestions that the mechanism for the elaboration, for example, of digestive enzymes, may

likewise be the source of hormones and those little known intracellular enzymes upon which metabolism seems to depend (Bowen, '24a; Wilson, '25). It is, indeed, conceivable that an exact knowledge of the more obvious phenomena in gland-cells might carry us far toward an understanding of those less conspicuous but more important secretory phenomena which are the common property of all cells.

HISTORICAL ORIGINS OF THE PROBLEM

Das Blut enthielt in sich schon alle Bestandtheile aller Secrete präformirt.

(Statement of 18th century point of view by R. Heidenhain, 1883.)

Es sind . . . . nicht die Blutgefässe, welche secerniren, sondern die Wände der überall geschlossenen Drüsenräume, auf welchen die Blutgefässe ein Netz bilden. Die Drüsen stellen in ihrem Innern eine im kleinsten Raume construirte grosse Oberfläche dar; die diese bekleidende lebendige Substanz ist es, welche die Sekretion einleitet.

(Paraphrase by R. Heidenhain (1883) of the view of J. Müller, 1830.)

Car, pour nous tous, il est absolument évident que la sécrétion n'est pas un acte de simple filtration, comme on le croyait naguère, mais un phénomène essentiellement cellulaire, et que, si l'on savait ce qui se passe dans les cellules essentielles d'une glande, on connaîtrait parfaitement la fonction physiologique de cette glande.

(Ranvier, 1887.)

The production of fluid or semifluid material in connection with definite organs (glands) has of course long been known, and during the 18th century with the advance in general knowledge of the human body and its functions, a serious attempt to put glandular phenomena in harmony with other anatomical knowledge first emerges. According to Ruysch and others, there existed direct connections between the excretory ducts of a gland and the vascular system, the blood itself being presumed to contain preformed all kinds of secretory products. Depending now on the nature of the vascular arrangements, their length, width, etc., in this gland or that, specific constituents of the blood stream were separated out, squeezed by the pressure in the blood vessels through sieves of different apertures. For an extended exposition of these 18th century viewpoints, reference may be made to Haller, Elementa physiologiae II. liber VII, Lausannae, 1760.

Although opposed to the conclusions of Malpighi and many others, such views persisted into the 19th century, until J. Müller in 1830 arrived at a better understanding of the secretory process. Müller rejected the vascular theory and held that the active agent was the living substance which lined the walls of the glandular lumina, the blood-vessels merely forming a superficial network. Differences in the secretory product were traced to those differences in living substance familiar in organs of various kinds. The gross structure of a gland was dismissed as having no bearing on the essential problem.

At this point the cell-theory appeared, followed by immediate efforts to reduce glandular structure to a cellular basis (Henle, Müller, etc.), a result first clearly established by Dujardin (beginning in 1837), although Dutrochet already in 1824 had written, "la cellule est l'organe sécréteur par excellence." For an interesting historical review refer to Milne-Edwards ('72). From the work of the two following decades, it became gradually clear that glands are composed of cells in varied arrangements, although in Kölliker's *Mikroskopische Anatomie* of 1850, their relation to the secretory process was not yet resolved.

Coincident with these early attempts to correlate the cell-theory with glandular flow, was another development which had its origin in the work of Dutrochet and

Jolly on membrane-diffusion. The obvious possibilities of arriving at once at a physical explanation of glandular activity were eagerly grasped, and eventuated in the physical view developed by Ludwig in his *Lehrbuch der Physiologie* (1856).

It was peculiarly the contribution of R. Heidenhain ('66 to '83) to bring back into clear focus the essential part in glandular activity played by living substance —the individual cell—and to express this in terms at once useful to both cytologist and physiologist, avoiding a too facile mechanical explanation on one hand, and, on the other, an explanation which loses itself in obscure "vital forces."

THE INDIVIDUAL CELL AS THE BASIS OF GLANDULAR ACTIVITY

. . . dass die Sekrete kein Caput mortuum, sondern die Producte der chemischen Thätigkeit lebender Zellen sind.

(Nussbaum, 1877.)

En réalité, toutes les glandes, mérocrines et olocrines, présentent un mécanisme analogue de la sécrétion . . . . Ces termes de mérocrines et olocrines se rattachent à un processus qui caractérise plûtot une des phases ou un des modes de l'excrétion que la sécrétion proprement dite.

(Ranvier, 1887.)

That differences in the "contents" of gland-cells correspond in some way to differences in the excretion-products of glands was suggested by Henle in 1841, but the first clear proof that gland-cells actually contain part of the excreted material, visibly preformed, in the cytoplasm, was given by Goodsir in 1844, in case of the ink of cuttlefish, a case of special interest since secretions with a distinct color are not common in animal cells. (For a few examples see Solger ('94).) The further fact that in sebaceous glands the cells become laden with fatty secretory products and that the ensemble is lost at the time of excretion was completely described by Kölliker in 1850. Many other workers (e.g., Leydig, '57; Schulze, '67) saw secretory products within the gland-cell and clearly recognized that they were subsequently extruded as an essential part of the familiar glandular products. Nevertheless, the general relation between preformed intra-cellular secretions and the visible products of an active gland was for many years a subject of controversy. For a proper appreciation of the difficulties which were encountered in early attempts to understand the exact connection between the product of a particular gland and the living material which constitutes its cellular substratum, it is necessary at this point to consider certain features of the excretion-process.

It is clear now, after long controversy, that gland-cells may evacuate their secreted contents in several different ways. As suggested by Ranvier's classification, there are two extreme types of behavior—holocrine and merocrine.

The simplest type is the holocrine gland, which has as a product the cells themselves with all their enclosed secretion. Such are the sebaceous glands of mammals, and avian oil-glands. In merocrine glands, on the other hand, the secretory products are released, washed out as it were, from the individual cells, which themselves are left to repeat the process. There are many intermediate conditions in which lobes of the cell-periphery, laden with secretion, are broken off in toto, as in mammary glands, certain Harderian glands, etc. This mode of excretion is often called "blasenförmige Sekretion" (cf. Henschen ('04), Mislawsky ('09), Brinkmann ('12), Schiefferdecker ('17), but it appears that this name has also been applied rather loosely to many cases in which the excretory processes are somewhat different, as for example the case described by Van Gehuchten ('90), often termed "tropfen-

förmige Sekretion." It is now clear that in the final analysis all these differences have little significance, for soon or late individual cells of the merocrine type "wear out" and doubtless also go to pieces to be lost in the general glandular product, their places being taken by new cells.

Unfortunately, to earlier workers the true import of the excretion-phase in holocrine and merocrine glands was entirely missed and the essential unity of secretory phenomena was obscured by the belief that the holocrine gland-cell is undergoing a degenerative process which reaches its culmination in the loss of the whole cell. This view was first sponsored by Virchow ('57), who compared the fatty material in a sebaceous gland to the products of "fatty degeneration" familiar to pathologists. Brinkmann ('12) and others before him have even been led by this interpretation to consider the exclusion of sebaceous glands from the category of "true" glands, holding (Brinkmann) that the fatty material results from necrobiotic changes due to unfavorable relation to sources of oxygen and food. This whole phenomenon, according to Brinkmann, is to be contrasted with the "vital" processes in other gland-cells—whatever that may mean. In any event, the nature of the cell-cycle having been so early and so clearly made out in these typical holocrine cells, it was natural that somewhat similar views should arise in explanation of the phenomena in other glandular types (e.g., in goblet-cells, Schulze, '67). And, as a matter of fact, it has since become evident that the holocrine type of behavior is by no means limited to glands of lipoidal secretion.

From such a background emerged the view originally held by R. Heidenhain ('68), that the gland-cells become filled with secreted material, which is discharged together with the cell when the gland becomes active, cell and secretion being washed out by the fluid which, released from the capillary stream, forms the substratum of the glandular discharge. In other words all gland-cells would in the final analysis belong to the holocrine type. Or as Ogata ('83) put it, the gland can only function as it destroys certain cells and builds new ones in their stead. These views are in essence only an extension of Cl. Bernard's old theory of living processes, according to which the cell builds incoming materials into living protoplasm—a part of itself—and differentiations then emerge only by transformation of the living substance proper. Pflüger ('66), on the other hand, held that the gland-cell produced secretions from which it freed itself at stated moments, returning then to its primitive condition to repeat the cycle of storage and discharge. The living protoplasm itself was not directly transformed into secretion-product (cf. Galeotti ('95), Krause ('95), Kolossow ('98), etc.).

The ensuing controversy expressed itself in a voluminous literature, summaries of which can be found in Van Gehuchten ('90), Galeotti ('95), and Oppel ('00), and even today the excretion-process in those gland-cells which are not obviously of the holocrine type, is in many cases incompletely known. However, the key to the matter was found by a pupil of Heidenhain, Lavdovsky ('77), who concluded that glandular activity (in merocrine gland-cells) involved features of both views. Thus he held that gland-cells were maintained in normal activity (in Pflüger's sense) for a longer or shorter period, but were in the end of a "transitory" nature and must finally be lost with the excretory product. The actual discharge from a gland-cell of the secreted material and the correlation of the fluctua-

tions in amount of secretion contained in the cell with different phases of secretory activity, were finally demonstrated by Langley (and Sewall) in a long series of papers dating from 1879. In its essentials this represents our present conception of cellular history in merocrine glands, the actual length of life of a given cell and the exact method of replacement being still very imperfectly understood.

Thus have modern views of the gland-cell gradually taken shape. It is now clear that the gland-cell is in reality a "secretory" cell, which lends to the glandular products their characteristic essence through the intermediary of chemical transformations effected in some way within the cell itself. The general course of events is presumably based upon a common pattern, and to this extent all gland-cells are but variations of a single cell-type. The superficial differences which gave rise to the terms holocrine and merocrine, refer not to the secretory, but to the excretory, activities of the cell. And to this extent these terms apply to a physiological rather than a cytological problem. In all cases there is deposited in the cytoplasm of the gland-cell, as a product of cellular activity, a characteristic secretion-material. This is then discharged by the loss of the whole cell (holocrine type), or is "washed" out of the cell together with an abundance of fluid abstracted from the vascular stream, the living cell-substance proper remaining behind essentially intact (merocrine type).

I ought perhaps to digress at this point from the main course of the discussion to point out that in many holocrine glands (sebaceous type) the "degeneration-theory" is still too widely accepted as an explanation of their activity. It therefore seems worth while to emphasize the fact that the data now available provide a conclusive demonstration of the inadequacy of any such view. Secretion in a sebaceous gland-cell is a synthetic process essentially akin to that in mucous or serous cells. This was first clearly indicated by the classical studies of Altmann ('94), whose main conclusion has been corroborated by many later workers (Michaelis ('98), Ottolenghi ('01), Bab ('04), Stern ('05), Kuć-Staniszewska ('14), Ludford ('25b), Bowen ('26b)). It is high time to abandon the outworn catchwords of "fatty degeneration" as an explanation of the secretory phenomena in sebaceous glands.

THE MORPHOLOGY OF SECRETION

Eine merkwürdige Erscheinung bei der Umwandlung des Zelleninhaltes ist, dass häufig die Bildung gewisser Sekrete in eigenen, innerhalb der Zelle liegenden Bläschen, den "Sekretbläschen" erfolgt.

(Leydig, 1857.)

Alle Beobachtungen . . . . bestätigen daher den einen Satz: Die Secretion ist ein granulärer Process . . . .

(Altmann, 1894.)

When gland-cells are studied in the fresh condition, or after fixation and staining, their microscopic appearance varies with the kind of cell and the method of preparation. To most earlier workers the morphological details of a gland-cell seem to have been of little interest, and they speak rather casually of the "contents" of the cell as clear, transparent, granular, a network containing vacuoles, etc.; and they refer the origin of such appearances to "schleimige Metamorphose," "dégénérescence muqueuse," "fatty degeneration," and the like. It was clearly recognized that chemical changes within the secretory cell found expression in various morphological appearances of the cytoplasmic area. These appearances were particularly commented upon during the period between Heidenhain's initial work (1866–68) and the development of Altmann's granular theory, which reached its final

expression in 1894. The results of this period are exhaustively reviewed by Oppel ('00) for the glands of the buccal cavity and the pancreas; by Paneth ('88) in case of goblet cells, and by Nicolas ('92) and Galeotti ('95). The occurrence of definite granules in the pancreas-cell had been noted by many observers since 1850 (at first under the name of fat granules), and a granule-structure was also observed particularly by Langley ('79–'89) in serous and mucous cells (salivary). Langley, Heidenhain, and Nussbaum ('77–'86) observed cells in both the living and fixed condition, and came to the conclusion that the granules represented secretion-products which were evacuated during the excretory activity of the cell, and were in some sense the source (after dissolution) of the characteristic qualities of the fluid from a particular gland. The first complete account of this phenomenon was the work of R. Heidenhain ('75) on the pancreas. In 1879 Langley wrote, "That is, during secretion the granules normally contained by the cells, are in some way or other used up, probably to form part of the saliva [in this case] secreted." See also Kühne and Lea ('82). It is, however, to be noted that it is not necessary to suppose that in the pancreas, for instance, the zymogen granules are themselves the forerunner of the pancreatic enzymes, but are merely the physical substratum in which the inactive enzymes are somehow contained (e.g., Lewaschew, '85). Similar views were espoused by many other workers during the period from 1880 to 1890—for example, the "Sekretbläschen" of Leydig ('57), the "Drüsenkörner" of Schwalbe ('72), the "Sekrettropfen" of Platner ('89), Paneth ('88), and the "Primärgranula" of M. Heidenhain ('90). An extended list of similar references will be found in Galeotti ('95), Nicolas ('92); also Müller ('96). Nevertheless the whole matter remained in a somewhat chaotic state due primarily to the fact that while in some glands, like the pancreas, the granular condition of the secretion is readily demonstrated, in other glands (mucous cells in particular) the granular appearance is usually obscured.

The real nature of the secretion-process was first clearly elucidated by Altmann, whose extended observations established the occurrence in the cytoplasm of discrete granules (or vacuoles) as the universal characteristic of secretory cells. Altmann ('94) concluded that secretion is always a granular process and subsequent observation has led increasingly to the establishment of this opinion as the correct explanation of gland-cell morphology. An excellent historical sketch of the emergence of this, the so-called "Granulalehre" as applied to gland-cells, is given by M. Heidenhain ('07), pp. 333 et seq. The facts were, indeed, already in process of clear generalization in 1899 (Harrington). Papers of this period in which the granule doctrine emerges with varying degrees of understanding are those, for example, of Nicolas ('92), Saint-Remy ('92), Nicoglu ('93), Galeotti ('95), Müller ('96), Solger ('96), Weiss ('99), Ellermann ('00), Noll ('01), Schmincke ('03), and Fleischer ('04).

The cytologist, therefore, finds it always possible to observe (at some stage) in a gland-cell a congeries of "granules" which constitute the "secretion" produced by the cell. There are a few anomalous exceptions to this rule (e.g., Carlier ('05), Eklöf ('14), Benoit ('20), Saguchi ('20a)) in which unformed secretions have been described, but the status of these observations seems to me decidedly doubtful. When the gland excretes, the whole cell may be lost as in the holocrine type, or the granular area only may be swept out by a current of watery fluid passed through

the cell from the blood or lymph capillaries adjacent to its base. In some cases the granules are excreted intact, but in the majority of cases they are dissolved in the outgoing stream at the moment of excretion, or may undergo more or less fusion and "solution" (?) within the cell prior to the beginning of excretion. For an understanding of the secretory process, however, these variations are of secondary interest.

Specific attention should perhaps here be drawn to the fact that the "granules" are not necessarily the only cellular contributions to the excretion-product of a gland. Clearly, in holocrine glands, the product includes at least remnants of all the cell-structures. It is likewise probable that during excretion there is in all gland-cells some loss of the cellular substrate. Just what such cellular contributions will be in a particular instance, is probably to a certain extent a matter of chance. In any event, it has not been shown that they have any significant part to play in the glandular product as a whole; and the inclusion of fragments of the Golgi apparatus, chondriosomes, extruded nuclei, etc., seems quite lacking in the importance which some observers have attached to this phenomenon.

The exact method by which excretion itself is accomplished undoubtedly differs in different glands, as is sufficiently indicated by the mere occurrence of the holocrine and merocrine conditions. The problems thus raised fall, however, rather within the field of the physiologist than of the cytologist. For discussion of the views which have been proposed, refer, for example, to Ranvier ('86–'88), Van Gehuchten ('90, '91), Gilson ('90), Kolossow ('98), Mathews ('98), Zimmermann ('98), Henry ('00), Brinkmann ('12), Heidenhain and Werner ('24), and Benoit ('26). Here also may be noted the occurrence of so-called secretory capillaries which sometimes penetrate into the cytosome and presumably serve as extensions of the duct-system by which the glandular products are evacuated. For discussion of older literature on this subject see R. Heidenhain, ('83), and Kölliker ('89), and for the later work, Cajal ('89), Fusari and Pansci ('90), Golgi ('93), Müller ('92, '95, '98), Solger ('96), Stöhr ('96), Krause ('97), Kolossow ('98), Oppel ('00), Browicz ('02), Fleischer ('04), and Arnold ('08).

The morphology of the "granules" which are thus the essential product of secretion, has been little studied, and only very recently have the possibilities of a generalized analysis received adequate attention. These possibilities find their source in old accounts like those of Meckel ('46) and Leydig ('57), who observed the formation in certain secretory cells of definite, intracellular vesicles or vacuoles (Sekretbläschen). Altmann ('94) subsequently recognized that his secretory grannules were often divisible into a central substance and a peripheral layer (or vacuole). A similar state of affairs seems to have been partially grasped by Nicolas ('92), who described the secretion-bodies as vacuoles (of liquid content) each enclosing a granule (see also Flemming ('82), Stöhr ('87), Held ('99), Fleischer ('04)). These scattering observations were finally brought to a focus by Renaut ('07), who undertook an analysis of the structural details of secretions, which he subsequently ('11) embodied in a very readable account of secretory processes. He pointed out in the first place that the simplest type of secretory activity was expressed by the formation and growth of a vacuole or droplet of permanently homogeneous material, fluid or semi-fluid in nature. This, Renaut termed the plasmocrine mode of secretion. A more complicated method

involves the formation of a minute granule around which a vacuole forms, and as the vacuole enlarges it serves as a minute reservoir in which specific products of cellular activity are accumulated and gradually concentrated by addition to the central granule. This granule he called a "grain de ségrégation," and the whole process constitutes the rhagiocrine mode of secretion (fig. 1). Still other modes of secretion were defined in his paper, but these seem of decidedly less general interest.

It is now becoming increasingly evident that secretion is essentially a vacuolar phenomenon, the great majority of cases

vary glands the enclosing vacuole may be retained for a long period, perhaps permanently (e.g., Bowen, '26a). Not infrequently the granules go through a process of ripening or maturing, often involving special features of morphology and staining capacity (e.g., Altmann, '94; Heidenhain, '07; Bowen, '26a, etc.).

This duplex structure of each secretory droplet has been recently interpreted in general terms by Parat ('28), Bowen ('26d), and others, in the following manner (fig. 1). The vacuole first arises as a watery droplet separated from the rest of the cell-substance by a limiting surface-membrane of some kind. Across this

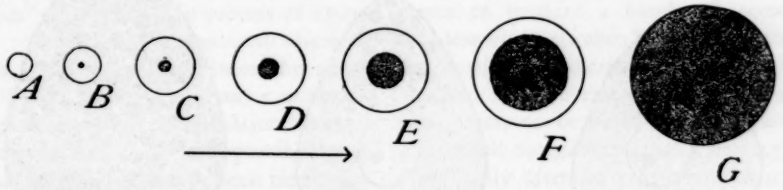

FIG. 1. PROGRESSIVE SERIES OF STEPS IN THE PRODUCTION OF A SECRETORY DROPLET OF THE RHAGIOCRINE TYPE

The secretory granule proper is stippled; its size with respect to the enclosing vacuole has been drawn somewhat too small in order clearly to bring out the topographical relations. In many cases the granule may be eccentrically placed within the vacuole, a condition not shown in this diagram.

resulting in the production at some stage of a central granule (rhagiocrine mode). Clearly the "granules" of older workers were sometimes secretory vacuoles in which the granules proper were not demonstrated, in other cases the granule alone was demonstrated, and in some cases the ensemble was correctly made out. In serous cells, the granule-within-a-vacuole structure is often easily demonstrated, while in mucous cells special staining is usually required. Furthermore, the growth of the granule may continue until it fills the entire vacuole, which is itself obliterated (fig. 1 *G*). This occurs very quickly in the vertebrate pancreas, while in the serous cells of many kinds of sali-

membrane pass secretory materials which have been elaborated by cellular activity and, becoming concentrated within the vacuole, are finally deposited in the form of the familiar "segregation granule." In this simple procedure the morphological essentials of secretory phenomena seem at last to have found an adequate basis.

Finally, with respect to the physiological interpretation of the origin of secretions, two views have been held, based to some extent on an author's opinion as to whether glandular excretion involves the total breakdown of the cell or not. According to one view, derived from Claude Bernard's theory of vital activity, the secretory droplets arise by direct chemical

transformation of protoplasm. According to the other view, well expressed by Pflüger ('66), the gland-cell builds secretory products through the intermediary of a special synthetic activity, being then capable of freeing itself at definite times of these products, whereupon the cell returns to its original condition and repeats the process. Or as Haeckel expressed it, the cell behaves like a plast. Not only does this second view of secretion seem necessitated by modern trends in the theory of cellular physiology, but, as will later appear, it is the only view in harmony with the morphological findings.

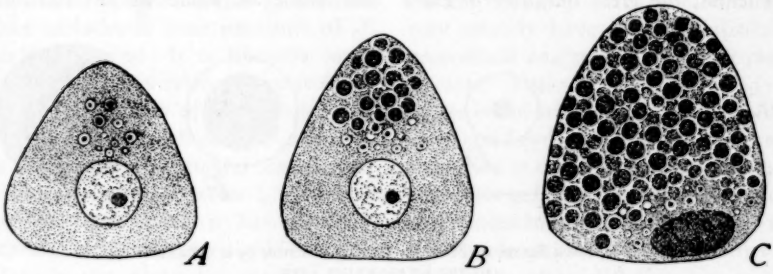

FIG. 2. SUCCESSIVE STEPS IN THE SECRETORY CYCLE OF A GLAND-CELL (DIAGRAMMATIC)
A, first appearance of secretory products at the beginning of a cycle of synthetic activity; *B*, intermediate stage in the formation of secretory droplets; *C*, final stage, shortly before excretion begins.

THE SECRETORY CYCLE

> In denjenigen Drüsen, bei welchen Perioden der Thätigkeit mit Zeiträumen der Ruhe abwechseln, lassen die secernirenden Zellen Unterschiede ihres innern Baues erkennen, welche für den ruhenden und den thätigen Zustand charakteristisch sind. . . . Zu bestimmten Zeiten nimmt die Zelle aus dem allgemeinen Ernährungsmateriale des Blutes oder vielmehr der Lymphe bestimmte Substanzen auf, zu bestimmten Zeiten setzt sie dieselben in bestimmter Weise um, zu bestimmten Zeiten giebt sie die Umsetzungsproducte nach Aussen hin ab.
>
> (R. Heidenhain, 1883.)

That gland-cells must pass through internal changes, which in their totality comprise a "secretory cycle," eventuating in the discharge of a secretion, was early recognized in case of sebaceous glands and others which were supposed to be of a similar type (goblet cells, for example, Schulze, '67). But that all secretory cells exhibit changes in appearance correlated with excretory stimuli was for a long time unrecognized. It seems to have been hinted first by Claude Bernard in 1864, but it is generally agreed that the initial contributions to this problem were the classical papers of R. Heidenhain extending from 1866 over a period of fifteen years. Heidenhain, adopting a histophysiological approach to the problem, demonstrated that when a gland was stimulated its cells underwent a change in appearance, thus definitely proving for the first time in many kinds of glands that secretory activity is directly linked with activities of the cells themselves. The real nature of the change was further elucidated by Lavdovsky ('77) and particularly by Langley ('79, etc.), not to mention the work of many others, an extensive bibliography of which is given by Oppel ('00).

It is now clear that in the beginning the cytoplasm of a gland-cell is free from secretion-droplets. These presently appear in ways characteristic of different glands, and increasing in number and size give to each gland-cell its characteristic histological appearance (fig. 2). Finally, in case of holocrine glands, the cell gorged

with secretion is extruded bodily, while in case of merocrine glands only its secreted contents, either in part or in whole, are expelled. The cell in the latter case then resumes its secretory synthesis. Thus the cell passes through a "cycle," which obviously may or may not be repeated (fig. 3). As Van Gehuchten ('90) clearly pointed out, the cell in typical cases passes from a condition of "rest" into a state of active secretion, thence to the phase of excretion, and so back to the original "resting" state. Here again physiological terminology disagrees with the facts of morphology, for the physiologist calls that cell at "rest" which is synthesizing its secretion-product, and applies the term "active" only to cells in process of excretion. Fortunately these contradictions are of little importance since the terms "rest" and "active" are in any event cytological misnomers. The relation between secretory activity and the possibility of mitosis in gland-cells has been much discussed, but its consideration falls beyond the scope of this review. As an introduction to the literature, see for example, Peter ('25).

As a matter of fact, the secretory cycle of the individual gland-cell has received little attention, and its exact nature is still in many cases uncertain (see Bowen, '26a). Clearly in holocrine glands the cycle is very definitely marked. Beginning with an "undifferentiated" cell, the secretion-droplets begin gradually to appear, finally filling the cytoplasm, and the cycle closes with the extrusion of the whole cell. There are other cases in which small aggregates of the secretion are in one way or another "budded" off from the cell-periphery. Examples are found among many glands of lipoidal secretion (R. Heidenhain ('83), Nissen ('86), Altmann ('94)); also the phenomenon of "Pfropfbildung" (so named by Schulze ('67)) or "blasenförmige Sekretion" (van Gehuchten ('91) (?), Henschen ('04), Mislawsky ('09), etc.). This may presumably continue for a longer or shorter period, new secretory droplets being constantly synthesized and moved toward the periphery for excretion. Finally, however, it seems certain that the cycle closes with the loss of the cell as a whole. The end-result is the same as in the strictly holocrine gland-cell, but there is interpolated a long period during which the casting off of cellular fragments loaded with secretion is balanced by a continual synthesis of new droplets. There are other cases, as for example the parotid gland of the cat (Altmann, '94; Bowen, '26a), where under normal circumstances the cell seems to produce a batch of secretory droplets which are then "ripened" without any further significant addition to their number. The entire secretory content then seems to be expelled, the remnant of the cell reorganizing for a new cycle. Presumably after an indeterminate series of such cycles, the cell itself is finally lost ("wears out").

There is, accordingly, in many secretory cells an all-or-none type of response. The cell is not normally prepared to excrete any of its contents until the whole is ready. The special cases just noted are variations which in many ways suggest another type of cycle that is of frequent occurrence. In this case (the tear gland, for example) the cells become gorged with secretion and upon stimulation excrete the more peripheral portion, while the synthetic processes continue undisturbed in the more deeply lying part of the cells. The end-result is not unlike that in some of the cases already noted, except that the secretion-products are, as it were, partially washed out of the cell, instead of being budded off in cellular fragments. And in these cases the rhythms in the cycle are not terminated by a clear-cut all-or-none

response, such as often occurs in other glands.

THE ORIGIN OF SECRETION-DROPLETS

Having thus traced the development of opinion concerning glandular activity in so far as this can be formulated in cytological terms, we arrive at the conclusion that the problems of glandular cytology center in the origin of an individual secretory droplet. One of the first discussions of this problem in which the true significance of the facts was broadly recognized and clearly formulated is given by M. Heidenhain, in his *Plasma und Zelle* ('07). In the beginning it was considered satisfactory to explain the origin of secretions as due to mucous or fatty degeneration (e.g., Virchow ('57), R. Heidenhain ('68), etc.); or as related in an indefinite way to theories of protoplasmic structure (Schiefferdecker, ('84), Mislawsky and Smirnow ('93), Ver Eecke ('95), Carlier ('96), Hammar ('97), Montgomery ('98), Harrington ('99), Pacaut and Vigier ('06), etc.). During the eighties of the last century, however, attention began to focus more sharply on this essential problem of secretory origins. In the intervening half-century literally scores of conflicting cytological explanations of secretory synthesis have been presented. In the remaining portion of this review, I wish to discuss the general results of these investigations and to attempt some critical estimate of our present knowledge. The measure of the probability of a particular interpretation must obviously be the ability of a set of observations to account for the origin of a single, individual, secretory droplet.

For convenience in handling the vast mass of accumulated material, I shall begin the discussion with those views which find a center for secretory activity in the nucleus; and thence I shall pass over into the cytoplasmic aspects of the problem.

THE RÔLE OF THE NUCLEUS IN SECRETION

> Daraus ist die eigenthümliche Ausbildung des Kernes in diesen kolossalen Zellen [der Raupenspinngefässe] zu erklären. Der Kern verästelt sich durch die Zelle hindurch, um überall seinen Einfluss geltend zu machen und die Sekretion zu vermitteln.
>
> (Meckel, 1846.)

> Dies spricht dafür, dass der Kern vor allem für die secretorische Function der Zelle eine besondere Bedeutung hat.
>
> (Korschelt, 1889.)

> Les recherches minutieuses faites sur cette question prouvent que le processus sécrétoire du noyau, que la participation du noyau à la sécrétion protoplasmique peut se faire suivant un mode assez variable et d'une façon plus ou moins évidente.
>
> (Maziarski, 1910.)

One of the most widespread and deep-seated beliefs in zoölogy seems to be that the nucleus is the source of enzymes and secretions generally. It is argued, on grounds either of theoretical necessity or direct observation, that materials pass from nucleus to cytoplasm, there to become secretions. This theory requires, as a fundamental basis, the transfer of material from cytoplasm to nucleus and vice versa. That such exchanges must occur in any event seems rather obvious and the enormous growth of the nucleus during development of an egg, or during the reconstruction-stages following mitosis, is ample evidence that materials must pass into the nucleus from the surrounding cytoplasm. It is generally agreed that such contributions are made through the nuclear membrane in soluble form, and not by the penetration of formed material, although some exceptional accounts in the older literature are cited by Korschelt ('89); (see also Montgomery ('98)). With respect to the passage of substances from nucleus into cytoplasm, there is much disagreement, as noted later in more detail, but demonstrative evidence of the

passage of material from the nucleus, as indicated indubitably by decrease in nuclear size, is rather scanty. Nevertheless the fact should not be lost sight of that during mitosis the bulk of the nuclear content is cast out directly into the cytoplasm, and such being the case, there seems no adequate reason why nuclear emissions might not also occur during the interkinetic phase. (See also, for example, Korschelt ('89), and the more extended discussion on page 316.)

The view that the nucleus is the primary agent in cellular synthesis was clearly formulated by Claude Bernard in 1878, although the idea had been variously expressed by his predecessors. Evidence for this view is now frequently based upon experiments in subdividing Protozoa, such as were first made by Nussbaum in 1884 and subsequently substantiated by Gruber, Balbiani, Hofer, and many later workers, extended discussion of which may be found in Nussbaum ('86), Henneguy ('96), page 451, Wilson ('28), page 657, and especially Sokoloff ('24). The results of Wallerian degeneration in nerve fibers, and changes in nuclear appearance in gland cells, and the work of Spitzer ('97), Loeb ('99), and Lillie ('02) on the nucleus as an oxidative center—a view now largely abandoned—have also been held to confirm the view that the nucleus plays the decisive rôle in operations of synthetic metabolism. That the nucleus coöperates in cellular synthesis would hardly be denied by anyone, but the prevailing opinion as to the importance of the nucleus seems to have been emphasized beyond the point justified by the facts. That a non-nucleated cell-fragment will not behave like a nucleated piece might be guessed in advance from modern conceptions of the cell as a system. But it does not follow that, because the behavior of two fragments can be correlated with their nuclear content, the nucleus must perforce be the all-important element of the cell. We have rather proved that the nucleus is a necessary part of the cell and that when the cellular system is upset by its removal, disaster is the only possible result. It is at least possible that if some of the cytoplasmic components could be removed, the remainder of the cell, even though nucleated, would never effect a complete recovery. Indeed exactly this result is reported by van Wisselingh ('08), who, by centrifuging filaments of *Spirogyra*, obtained fragments with a nucleus but very little of the chromatophore. Such cells could not effect their own reconstruction even though the nucleus was present. It is interesting also to recall Whitman's ('88) views, which sound almost contemporary. According to Whitman, nucleus and cytoplasm form a physiological unit, which must disappear once the unity is destroyed—that is, when nucleus and cytoplasm are separated. Quoting Whitman (p. 37–8): "Allowing that regeneration is impossible in the absence of a nucleus, that is no proof that the nucleus is the sole seat of regenerative power, nor is it proof that the nucleus is a more important factor than the cytoplasm." (Compare also Verworn ('91).)

Such being our uncertain position in respect to the general possibilities of the nuclear rôle in secretion, it is next in order to examine the actual result of cytological investigation of the nucleus in gland-cells. There are, in the first place, indices of nuclear coöperation in secretion which might supply valid evidence of activity without giving any specific indication of the exact part played by the nucleus. Such indices involve the assumption that material, elaborated within the nucleus in soluble (and therefore invisible) form, passes through the nuclear membrane by diffusion, to become in the cyto-

plasm a part of some visible secretory product. In the second place, it is conceivable that the nucleus might produce formed materials which would be extruded bodily, or else passed out by diffusion after prior solution (compare, for example, Macallum ('91), Maziarski ('10)). In one or both of these possibilities we must look for evidence of nuclear coöperation in secretion.

ein sekundäres Eingreifen des Kernes auf Grund seiner regenerativen Potenzen ohne weiteres ein und hiermit mögen eventuell gelegentlich auch Veränderungen des Kernes in Bezug auf Form, Volumen, Wechsel der Färbbarkeit etc. Hand in Hand gehen.

(M. Heidenhain, 1907.)

The first clear-cut accounts of changes in nuclear appearance correlated with the secretory cycle were given by R. Heidenhain ('66, '68, etc.) and his pupils, particularly Lavdovsky ('76). Thus, in the parotid gland of the rabbit, Heidenhain found the nuclei, in cells loaded with secretion, to be irregular (jagged) in outline with no nucleoli visible, while in early phases the nuclei appeared rounded-out and nucleoli could be discerned. Similarly, in the orbital gland of the dog, Lavdovsky found the nuclei flattened against the basal wall of the cell, while after excretion, they rounded-up and

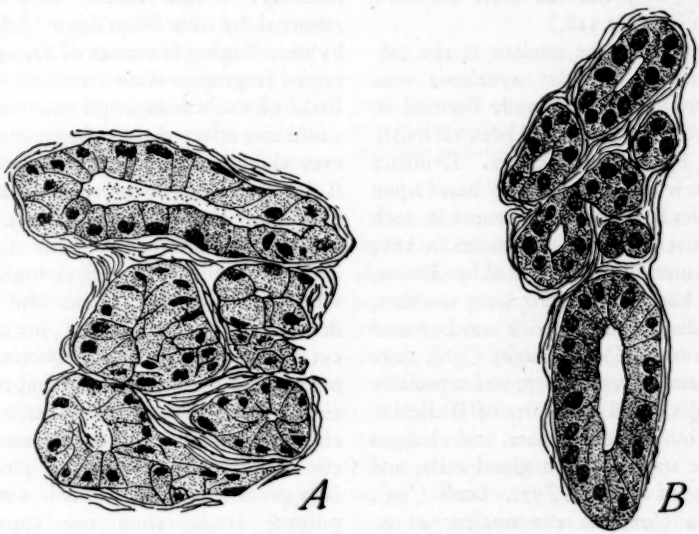

FIG. 3. CHANGES IN APPEARANCE OF GLAND-CELLS BEFORE AND AFTER EXCRETION—AS SEEN BY EARLIER WORKERS (LACHRYMAL GLAND)

A, before excretion—cells large and clear, with flattened, angular nuclei; *B*, after excretion—cells smaller, more granular, with large rounded nuclei which occupy a more central position in the cells. From Reichel, 1880.

Shape, Size, Position, and Staining Capacity as Evidences of Nuclear Activity in Secretion

Mit der Betheiligung des Kernes an der Thätigkeit der Zelle ist eine Veränderung seiner Structur verbunden.

(Korschelt, 1889.)

Wir kommen also im ganzen darauf zurück, dass eine direkte Mitbeteiligung des Kernes an der Sekretion oder der Erzeugung der Granula bisher nicht mit Sicherheit nachgewiesen wurde; dagegen räumen wir

moved into a more central position. Like changes in gland-cells of many kinds were noted by many later workers (fig. 3) and one case of a branched nucleus, very rare among vertebrates but not unusual in invertebrates (cf. p. 313), is cited by Carnoy ('84) in *Chelone*. Schmidt ('82) summarizes these changes, noting the differences in nuclear shape, size, position and staining capacity before and after excretion. The older literature is well reviewed by Korschelt ('89). Cases of variation in the chromaticity and other general morphological features of the nucleus in more recent literature are noted by Nicolas ('91), Carlier ('99), Henry ('00), Regaud and Policard ('01), Regaud ('02), Launoy ('03a), Fuchs ('04), Hoven ('12), Eklöf ('14), Jirešova ('18), Dolley ('25), Benoit ('26), Urasov ('27, '28), etc. Noll ('01) observes that some of these changes are discernible only after fixation and staining. An excellent tabulation of the older results is given by Mathews ('99); and later summaries by Garnier ('00a), Launoy ('03b), Laguesse ('05–6), and Benoit ('26).

It should be noted that these conclusions have been drawn from the study of vertebrate gland-cells, where nuclear changes during the secretory cycle are at most relatively inconspicuous, and there is indeed no agreement that such changes as do occur are necessarily indicative of nuclear participation in secretion. Korschelt ('89) in particular was disposed to accept the nuclear changes as circumstantial evidence of nuclear complicity in secretion, and a similar view has been taken by many writers down to the present time (e.g., Launoy, '03a; Jirešova, '18; Conklin, '24; Benoit, '26, etc.). Others, notably Nussbaum ('82), have held that these changes are due primarily to compression of the nucleus by the accumulating secretory granules. In other words, the changes in appearance are largely of mechanical origin, and tell us little about the actual function of the nucleus in a gland-cell (Kolossow, '98; M. Heidenhain, '07; Bowen, '26; and also List, '86); are merely evidence of the metabolic activities common to all cells (Gurwitsch, '04); are indications of "regenerative" activity (M. Heidenhain, '07); or represent regressive metamorphoses (Hermann, '88) or degeneration (Henry, '00). Mathews ('99) could find no periodicity in chromatic changes of the nucleus, while Garnier ('00) concluded that the changes followed no recognizable rule, and Launoy ('03a) interprets changes in nuclear size and position as "passive."

In invertebrate gland-cells, the nuclear behavior is often very remarkable, particularly with respect to the shape of the nucleus and to some extent its stainability. The best known examples are the spinning glands of insects, especially Lepidoptera. In these cells the nuclei are at first sensibly ovoidal, but subsequently they become extraordinarily branched so that each nucleus extends itself throughout the cell (fig. 4). These amazing nuclei, discovered by Meckel in 1846, have been studied by many workers (bibliographies in Korschelt ('89), Gilson ('90), Maziarski ('11), Kinney ('26), etc.). Even more remarkable are the nuclei in the spinning glands of *Cladius* (Korschelt, '89), and in the appendage glands of *Phronimella* (Mayer, '78). Other noteworthy cases are the nuclei in certain genital glands of *Branchipus* and the double-cells in the egg-follicle-wall of *Nepa* described by Korschelt ('89); also in the spinning glands of *Platyphylax* (Marshall and Vorhies, '06), and in isopod gland-cells by Conklin ('97) and Prenant ('97). Here the nuclei send out branching "pseudopodia" which are developed only on the side of the nucleus directed toward the accumulating

secretion. Still other examples of abnormal nuclear structure in invertebrates are cited by Korschelt ('89). Changes in the mere position of the nucleus are not conspicuous even in invertebrates (Korschelt, '89; Holz, '09). Variations in staining capacity are perhaps more suggestive than in vertebrates, but are rarely of striking nature. An extended series of observations (and discussion) bearing on the morphological changes in nuclei of isopod gland-cells is given by Maziarski ('10), and of other invertebrate gland-cells by Issakowitsch ('10), Maziarski ('11), Jörgensen ('13), Lutz ('21), Frankenberger ('23), Roskin ('25), and Millot ('26). Nevertheless, in spite of the remarkable nuclear conditions which certainly occur in many invertebrate gland-cells, it should be carefully noted that there are certain facts which may well cause us to hesitate in assigning over much importance to these "evidences" of nuclear participation in secretion. Thus Van Gehuchten ('90), in digestive cells of *Ptychoptera*, could find no evidences whatever of nuclear change; Krüger ('23) found no changes in reaction to basic dyes in the

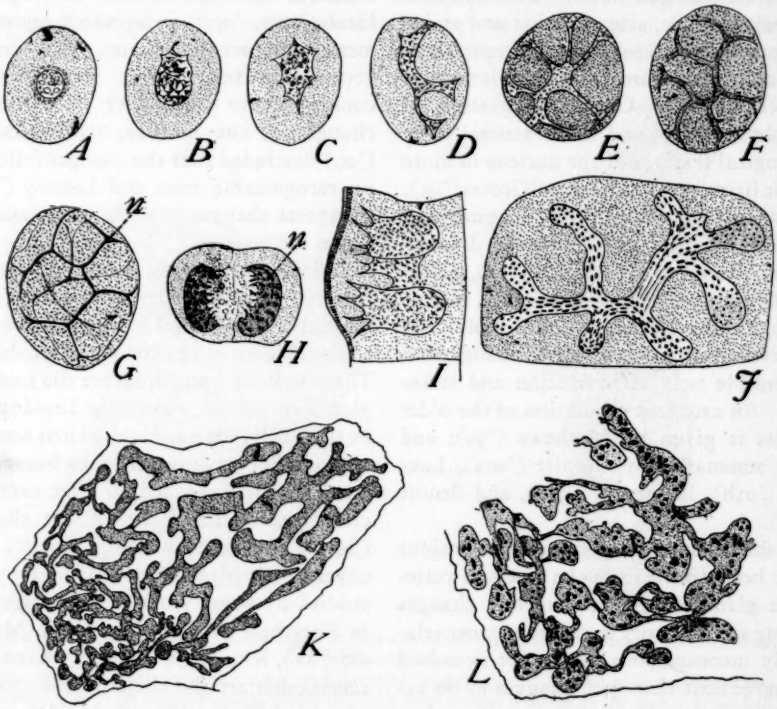

FIG. 4. MORPHOLOGICAL CHANGES IN THE NUCLEI OF ARTHROPOD GLAND-CELLS

A to *G*, in spinning glands of the larva of *Cladius*; *H*, "double-cell" gland in the genital apparatus of *Branchipus*; *I*, *J*, profile and plane view respectively of spinning gland-cells in the fresh condition, from the butterflies *Vanessa* and *Pieris*; from Korschelt, 1889.—*K*, a cell from the spinning glands of the larva of *Platyphylax* (nucleus stippled), and *L*, detail of a portion (lower left corner) of the nucleus of the cell in *K*; from Marshall and Vorhies, 1906. *n*, nucleus.

cement-glands of *Scalpellum;* while Gilson ('94) and Conklin ('97) find evidences that "nuclear pseudopodia" are merely the result of the mechanical indentation of the nuclear wall by the accumulating secretory droplets, and Murlin ('02) later concluded that they were fixation-effects, being entirely lacking in the living cell. Millot ('26), in certain glands in spiders, found no changes in nuclear shape. Further, Marshall and Vorhies ('06) found that the branching nucleus in the spinning gland-cells of *Platyphylax* showed no variations in shape corresponding to differences in secretory activity induced by experimental means. Finally, Seeliger ('00) has described in the muscle cells of the tail of appendicularians a most astonishing branched nucleus, where presumably no special secretory activity is involved.

Beyond the fact that the nucleus varies slightly in size, being smaller in cells gorged with secretion (according to R. Heidenhain and his pupils), conspicuous differences in volume are very unusual. Conklin ('24) reports that in *Crepidula* the nuclear volume in a liver-cell filled with secretion is only one-fourth as great as in a cell without secretion. This is taken to prove that during secretory synthesis, substances pass from nucleus to cytoplasm. Additional evidence is cited by Lukjanoff ('98), Phisalix ('00), and Schreiner ('18); but Launoy ('03a) considers that size-changes are merely passive.

On the basis of all these changes during a secretory cycle, the conclusion has been repeatedly drawn that the nucleus partakes in an important way in secretory activity. This view was carefully developed by Korschelt in 1889, and it must be said that little of a substantial nature has since been added. So far as vertebrate tissues are concerned, the argument for a direct connection of the nucleus with secretory synthesis is not particularly convincing. Too often the nucleus behaves outwardly as though it were unconcerned with the changes occurring in the cytoplasm. Certainly nuclear phenomena sufficiently marked to arrest attention are uncommon. Among invertebrates, however, even allowing for the apparent contradictions mentioned above, the remarkable nuclear changes, particularly in shape, are difficult to explain except in terms of secretory coöperation. In so far, therefore, as the argument rests upon the superficial appearance of the nucleus, it might be concluded that the facts warrant a belief that nucleus and cytoplasm in some way coöperate in secretory synthesis, the necessary exchanges being invisible to the cytologist because their material substratum is in soluble form (compare Lutz ('21), Yamanouchi ('22), Dolley ('25), Benoit ('26), Bowen ('26d), Ma ('28), Jacobs ('28), and many others). Earlier accounts often interpreted the secretory rôle of the nucleus in some such simple and rather intangible manner. In the later literature, an attempt is occasionally made to interpret the phenomena in terms of the extrusion from the nucleus of soluble "prozymogen" (Macallum, '91), of chromatic material in soluble form (Henry, '00; Launoy, '03b; Goldschmidt, '05; Jörgensen, '13; Benoit, '26), of nuclear sap (Launoy, '03c), etc.,—attempts of purely speculative character. (See also the section on the Chromidia, page 321.)

In a few instances, especially in the older literature, secretions have been directly derived by a presumed transformation of the entire nucleus. Such extraordinary accounts now seem in the highest degree improbable. For examples, see Calmels ('82), Nissen ('86), Steinhaus ('88), Ver Eecke ('95), Michaelis ('98), Limon ('02), and others. In many cases where such transformations have been described, the cells are said to be binucleate.

Thus, one nucleus can be directly transformed into secretion-products, while the other one remains behind to continue the cycle. Binucleate conditions have been noted in many glands, for example, Calmels ('82), Frenzel ('85), Steinhaus ('88), Van der Stricht ('93), Harrington ('99), Aigner ('00), Limon ('02), Brinkmann ('12), Schiefferdecker ('17), and Parat ('28). Further, Gilson ('90) has reported silk-secretion within the nuclei of the lepidopteran spinning gland, and Browicz ('05) believed that he had demonstrated the active share of the nucleus in secretion through his observation of bilirubin within the nucleus of liver cells. In holocrine gland-cells, the nucleus is of course included in the excretory product, but this phenomenon obviously belongs in a different category.

The Nucleus as a Seat of Production of Visible Secretory Materials

Le noyau joue un rôle important dans les processus sécrétoires; il participe directement à la formation du produit de sécrétion. C'est la substance nucléolaire qui donne le matériel pour les processus sécrétoires.
(Maziarski, 1911.)

Es findet kein Austritt der "Chromidien" aus dem Kerne statt, und man kann auch keine Beziehung derselben zur Kernmembran feststellen.
(Kulmatycki, 1922.)

The real argument for the participation of the nucleus in secretion is, however, usually based on evidence less circumstantial in nature. The view has been widely expressed that the nucleus produces secretory materials in visible form, which are then extruded bodily (but sometimes only after solution) into the cytoplasm. General reviews of the evidence supposedly favoring such an opinion are given by Galeotti ('95), Henry ('00), Vigier ('00b), Launoy ('03b), Goldschmidt ('05), Prenant ('05), Laguesse ('05–6), Maziarski ('10), Krüger ('23), Benoit ('26), and Millot ('26). The first account of this phenomenon is that of Ogata ('83) in the pancreas, followed by many subsequent observations of similar phenomena. The results may be arranged in three groups according to the mode of origin of the secretion:—

1. Origin from nuclear substance of indeterminate identification.

2. Origin directly or indirectly from nucleoli.

3. Origin from the chromatin (chromidia, etc.)

1. The origin from the nucleus (the term being here used in a general sense) of secretory droplets, or of formed materials which precede them, has been occasionally described, although the results present no agreement in details and have rightfully found no acceptance. Thus Galeotti ('95, '97) describes in various amphibian glands the appearance within the nucleus of small granules which migrate into the cytoplasm and become secretory granules. Somewhat similar examples are supplied by Engel ('09) and Roskin ('25). Hammar ('97) believed that the granules arose from the nuclear sap, while Ikeda ('06) and Ziegler ('27) are entirely indefinite. Holz ('09) and more especially Greschik ('15), in the intestinal epithelium of *Nematus*, assert that all the nuclear constituents contribute to the formation of a great secretory vacuole which fills a large part of the original nucleus and is finally extruded from the cell. Here also may be noted the "nucléo-rouge" bodies recently described by Dehorne and Hosselet ('28a), which emerge from the nucleus and are said to give rise eventually to chondriosomes ('28b).

2. The nuclear component most frequently described as the source of secretory materials, is, however, the true nucleolus or plasmosome, of which one or many constantly occur in gland-cell nuclei.

Our ignorance of the real significance of the nucleolus is axiomatic, although many workers have made more or less hypothetical suggestions. Some of the work (cf. vom Rath ('95), Saguchi ('20a), Krüger ('23)) on the nucleolus as a structure supposedly associated with secretory phenomena, seems to have found its source in the so-called nuclear secretion-hypothesis of nucleolar function—a view associated particularly with the name of Haecker. Nevertheless, the theories which attempted to define the functional significance of the nucleolus in generalized terms seem to have had little influence on workers interested primarily in gland-cells, and conversely the results obtained by students of secretory problems have never been accepted as decisive indication of the function of nucleoli in general. In secretion-studies, the variations in described behavior of nucleoli are extraordinarily diverse. Not only do the nucleoli vary in the supposed manner of their participation in secretory synthesis, but their origin, their mode of transportation across the nuclear boundary, and their behavior in the cytoplasm have been described in every possible way. Extended reviews of the nucleolar problems in gland-cells are given by Montgomery ('98), Vigier ('00b), Launoy ('03b), Prenant ('05), Maziarski ('11), Ludford ('22), Benoit ('26), and Millot ('26); and a paper by Hoffman ('02), dealing more particularly with the egg, and the classical paper by Korschelt ('89) contain much of interest.

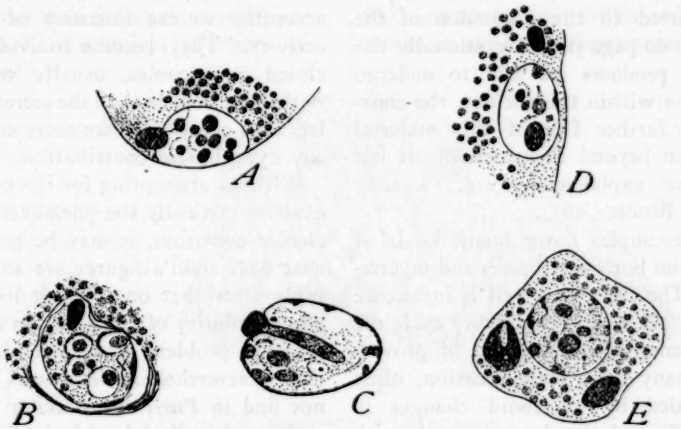

FIG. 5. VARIOUS STEPS IN THE SUPPOSED EXTRUSION INTO THE CYTOPLASM OF A NUCLEOLUS, IN THE PANCREAS OF SALAMANDERS

A portion only of the cell is shown in *A*, *B*, and *D*; in *C*, the nucleus alone, still in contact with an extruded nucleolus. Secretory granules in the cytoplasm are stippled; nucleoli, solid black. From Ogata, 1883.

All of the accounts of nucleolar activity in secretion go back to the work of Ogata ('83), who first described the emergence of the nucleolus (fig. 5) (pancreas-cells), and its subsequent transformation into a cell loaded with secretion products ("Zell-erneuerung"). Since this work, which in some respects is obviously incorrect, the bodily extrusion of nucleoli or their products from nucleus into cytoplasm, where in one way or another they participate in the formation of secretion-granules, has been repeatedly described.

Examples are vom Rath ('95), Henry ('00), Vigier ('00a, '01), Maximow ('01), Launoy ('03b), Maziarski ('11), Nakahara ('17), Schreiner ('16, '18), Saguchi ('20a, b), Skowron ('22), Krüger ('23), Ludford ('25a), Kinney ('26), Millot ('26), Noel and Paillot ('27), Jacobs ('28), Beams and Wu ('29). Many additional examples, especially between the years 1885 and 1900, might be cited, in which the extruded nucleolus is said to become the so-called nebenkern (parasome, etc.). These have, however, for the most part been referred to the discussion of the nebenkern on page 320. Occasionally the nucleolar products are said to undergo dissolution within the nucleus, the emission and further fate of this material being then beyond the reach of all but speculative explanation (e.g., Launoy ('03b, c), Benoit ('26)).

These examples cover many kinds of glands from both vertebrates and invertebrates. The story they tell is in essence the same. During the secretory cycle the nucleoli enter upon a phase of growth and in many cases multiplication, often accompanied by amoeboid changes in shape, differentiation into materials with special staining characteristics, and many other structural modifications. Most workers have considered the nucleoli in gland-cells simply as plasmosomes; but a few (e.g., Vigier ('01), Guieysse ('07), Saguchi ('20a), Noel and Paillot ('27)) derive them specifically from chromatin. According to Saguchi ('20b) certain secretory products come from the nucleolini—a special part of the nucleolus. This material, however produced, is transported to the cytoplasm where it usually undergoes modification or union with cytoplasmic materials before the definitive secretion is formed (most of the cases cited above); or in rare cases may be ready for immediate excretion (Henry, '00; Maziarski, '11). The most remarkable case is perhaps that of the silk-glands of insects described in extraordinary manner by Maziarski ('11), and in part corroborated by later workers (cf. Nakahara ('17), Kinney ('26), Noel and Paillot ('27), Dehorne and Hosselet ('28a)). According to Maziarski, the branching nuclei (fig. 4) contain a host of nucleoli, which probably multiply by fission (Vorhies, '08; Maziarski, '11), thus maintaining the supply. These nucleoli are said to be extruded from the nucleus in several ways according to the intensity of secretory activity. They become individually enclosed in vacuoles, usually while still within the nucleus, and the secretory droplets thus constituted are excreted without any cytoplasmic contribution.

Without attempting for the moment to examine critically the phenomenon of nucleolar extrusion, it may be pointed out that Maziarski's figures are so compellingly clear that one finds it hard to see any possibility of mistake. In short, the secretion-problem seems indubitably settled. Nevertheless, Nakahara ('17) could not find in *Pieris* the striking phases of activity described by Maziarski, and although he found nucleolar extrusions, his figures are decidedly less concrete. Subsequently, Kinney ('26), in *Hyphantria*, finds evidences of nucleolar extrusion only in similarity of staining reaction between the secretory granules in the cytoplasm and the intra-nuclear nucleoli. But she adds, perhaps significantly, that the number of nucleoli is not reduced during secretory activity, as one might perhaps expect. Finally, Yamanouchi ('22), in the silkworm, categorically denies the occurrence of nucleolar extrusion. It may also be noted that Korschelt ('96) and Meves ('97) fail to mention nucleolar extrusions (similarly, Marshall and Vorhies ('06), and Vorhies ('08)). If such phenomena are

at all conspicuous or demonstrative, it is more than strange that two such observers failed to note them. Thus, in a case which may be chosen as one of the best possible examples of nucleolar participation in secretion, the actual facts turn out to be surprisingly equivocal.

Conclusions as to the secretory rôle of the nucleolus are further rendered doubtful by the lack of uniform or satisfactory descriptions of how nucleolar material gets through the nuclear membrane. Some authors have described a direct perforation of the nuclear wall (Melissinos and Nicolaides ('90), Ver Eecke ('95), Carlier ('96, '99), Vigier ('01), Launoy ('03b), Ferrata ('06), Walker and Embleton ('08), Benoit ('21), Skowron ('22), Ludford ('25a), Jacobs ('28)), the membrane sometimes presenting visible evidences of an actual tear or rupture, and sometimes not. According to Ogata ('83) the nucleolus may "bore" through the membrane; Krüger ('23) believes that the nucleolus exerts a solvent action on the nuclear membrane at the point of contact; nuclear contractions assist in the expulsion of the nucleolus according to Maziarski ('11) and Montgomery ('98); and the nucleus may be drawn out into elongate processes, from the tips of which the nucleoli escape (Petersen ('07), Maziarski ('11); compare also Engel ('09)). There are also a few cases in which definite openings in the nuclear wall seem to occur (Vigier ('00a)) (compare also Galeotti ('95) and the "Karyopyle" of Ikeda ('06)). Other workers find a sort of budding phenomenon (Platner ('89), Laguesse ('24), Ludford ('25a)); others report a thinning of the nuclear membrane and subsequent passage of (colloidal?) materials without leaving any trace of their exit (Lukjanow ('88), Guieysse ('07); while still others describe an apparent disappearance of the membrane at the place of discharge (Ogata ('83), Henry ('00), Holmgren ('02), Maziarski ('11), Nakahara ('17), Noel and Paillot ('27)). According to Vigier ('00b), a large vacuole may arise in association with the nucleolus, within which the secretory granules appear, escaping thence by nuclear rupture, and Urasov ('28) describes the direct transformation of a nucleolus into a great intranuclear vacuole in which the secretory droplets develop. Other cases of this kind are reviewed by Urasov ('28).

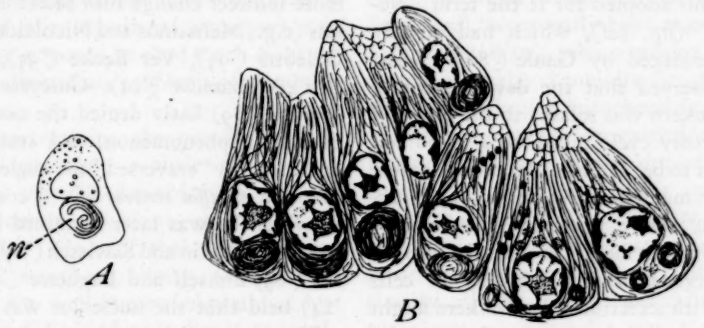

FIG. 6. THE NEBENKERN IN GLAND-CELLS

A, original figure from the pancreas of *Salamandra*, from Nussbaum, 1882; *B*, in the pancreas of the frog, from Mathews, 1899. *n*, nebenkern.

Before concluding the subject of nucleolar participation in secretion, the so-called

"nebenkern" (fig. 6) of some gland-cells should be mentioned. These nebenkern structures have been frequently associated with the ergastoplasm, which is separately considered in Section II. It is to be clearly understood that this structure in gland-cells (particularly the pancreas) has nothing whatever to do with structures of similar name in pulmonate germ-cells and in insect-spermatids. The nebenkern (parasome, paranucleus, accessory nucleus, etc.) in a gland-cell is a mass, often of fibrillar structure, the origin and meaning of which are still much in dispute. It was first described in gland-cells by Nussbaum ('82), who adopted for it the term "Nebenkern" (fig. 6*A*), which had already been introduced by Gaule ('81). Nussbaum observed that the development of the nebenkern was related to the phase of the secretory cycle in which a given cell happened to be, and like observations were made by many later workers. Cells engaged in active synthesis of secretory droplets were found to contain one or more large nebenkerns, while in cells loaded with secretion the nebenkern might be absent.

The history of this structure as a factor in secretory synthesis really begins with Ogata ('83), who first described its origin from a nucleolus which had migrated out of the nucleus. Its subsequent history was handled by Ogata in rather fantastic fashion (see also Ver Eecke ('95)), but the essential point here is his belief that the nebenkern is in one way or another the material basis of new secretory granules. For the next twenty years the literature of glandular phenomena was dominated by the nebenkern-conception. Since 1900, however, the importance of the nebenkern in gland-cells has received less and less emphasis, and the most recent studies scarcely mention it. The great interest formerly felt in the nebenkern produced numerous detailed and exhaustive reviews. To these reference should be made for a more adequate discussion than the present status of the matter seems to call for in this review. See, for example, Eberth and Müller ('92), Galeotti ('95), Henneguy ('97), Prenant ('98–'99), Mathews ('99), Garnier ('00a), Oppel ('00), Launoy ('03b), Laguesse ('05–'06, '24), Babkin, Rubaschkin and Sawitsch ('09), and Champy ('11). Following Ogata, however, quite a number of workers described the origin of the nebenkern or parasome by the direct extrusion of a nucleolus, followed usually by fragmentation or some more indirect change into secretory droplets (e.g., Melissinos and Nicolaides ('90), Galeotti ('95), Ver Eecke ('95), Vigier ('01), Maximow ('01), Guieysse ('07)). Platner ('89) flatly denied the occurrence of such a phenomenon, and stated that nucleoli only "traversed" the nuclear membrane in *paraffin sections* (!)—a contention in which he was later sustained by Babkin, Rubaschkin and Sawitsch ('09). Platner ('89) himself and Laguesse ('93, etc.; '24) held that the nucleolus was budded off in a lobe of the nucleus, but never actually penetrated the nuclear membrane. Others have traced the nebenkern structures to the cytoplasmic reticulum, ergastoplasm, etc., sometimes in combination with nuclear or other material (cf. Lukjanow ('87), Hammar ('97), Garnier ('00b), Babkin, Rubaschkin and Sawitsch ('09), Benoit ('26)). Garnier ('00a) in one case described the nebenkern as arising by transformation of an entire nucleus; and M. Heidenhain ('90) dismissed the nebenkern structures as products of degeneration. Pensa ('19) has recently given a discussion of these structures in terms of the physical state of the protoplasm in gland-cells.

On the whole, it must be confessed that the subject is in a very chaotic condition,

with little hope of immediate betterment. Certainly in many gland-cells there is no nebenkern present at any stage and there is much reason to believe that its appearance in fixed preparations was frequently due to faulty fixation (Morelle, '27a). Recent workers have been rather inclined to classify the nebenkern with the ill-starred ergastoplasm (see Section II), and to assign to it a minor place in the economy of a gland-cell (Benoit, '26). Some even of the older workers questioned whether it had any direct connection with the formation of secretory granules (Eberth and Müller, '92). It is my personal opinion that in the present state of our knowledge further study of the nebenkern structures can hardly be expected to shed much light on the more immediate problems of glandular cytology.

3. There remains the possibility that secretory granules, or their intermediate products, may be derived from the so-called nuclear reticulum—the linin and chromatin. Most of the work in this direction has been along the general lines of the well-known chromidial hypothesis of Goldschmidt ('05). According to this view, cytoplasmic differentiation is traceable to "trophochromatin" extruded (either directly or by osmosis) from the nucleus. The theory was not particularly developed by Goldschmidt in gland-cells, and he merely connected his general view with various structures previously described in gland-cells—particularly the ergastoplasm (see Section II). Other students of the chromidia were interested particularly in the egg, and gave little attention to gland-cells. The most extended paper is that of Erhard ('10) (see also Popoff ('10), Issakowitsch ('10), Dolley ('25)) who described nuclear extrusions which participated in various ways in the production of secretory granules. Older workers who connected the chromatin with secretion are Macallum ('91), Henry ('00), Conte and Vaney ('02), Launoy ('03b), Fuchs ('04), Carlier ('05), Nussbaum and Kulczycki ('06), and particularly Phisalix ('00); and more recently Maziarski ('11), Winiwarter ('25) and Benoit ('26). In some of these cases the secretion was described as arising within the nucleus directly from chromatin.

However, no very clear picture has emerged of how chromatin arrives at the end-stage of a secretory droplet, and accounts of different authors rarely present points of striking similarity. The present status of the chromidial hypothesis (together with a useful review of the literature) has recently been examined by Kulmatycki ('22), who comes to the conclusion that the chromidia (in *Ascaris* at least) are deformed mitochondria, and are not derived from nuclear extrusions. Jörgensen ('13) has likewise denied the extrusion of formed chromidia, and concludes that there is little evidence that the nucleus plays any definite part in secretion. It now seems clear that the attempt to classify all the formed materials in the cytoplasm as chromidia was a mistake, and to this extent interpretations of the chromidia in gland-cells are more properly referred to the special theories connected with the ergastoplasm, chondriosomes, etc. Similarly, accounts of secretion based on nuclear extrusions of very special kinds, may be considered in connection with the intermediate cytoplasmic products with which they were associated; as, for example, the views of Schreiner ('16, '18), Saguchi ('20a), and Laguesse ('24), Section II; and also the relation of the ergastoplasm to the nucleus, Section II; etc.

A Critique of Nuclear Function in Secretion

Daher leugnen wir im allgemeinen die unmittelbare Beteiligung des Kernes an der sekretorischen

Funktion und der Genese der Granula, schreiben ihm vielmehr ein regeneratives Vermögen zu.

(M. Heidenhain, 1907.)

Die Sekretion ist eine Folge der vereinten Tätigkeit von Kern und Protoplasma.

(Lutz, 1921.)

From this review, fragmentary though it necessarily is, it must be evident that attempts to derive secretions from the nucleus have been more characterized by their differences than their similarities. Workers, even on the same material, seem unable to corroborate details of what, one might suppose, would be very conspicuous features. This failure to reach some agreement could perhaps be cared for by the explanation that in different gland-cells a common method of secretion is not to be expected. But to many such an interpretation would seem quite impossible, and it would be more in accord with our views of organic unity to anticipate that phenomena occurring in one secretory cell would appear, though perhaps with varying degrees of visible emphasis, in all secretory cells. To what extent either of these points of view is upheld by available facts may perhaps be clarified by a brief analysis of the accumulated theories.

It will, I judge, be agreed that the bizarre accounts so common in the eighties and nineties must simply be traced to inadequate technique and outright errors of observation and interpretation. Similarly, practically no one now expects to find a solution in the behavior of the chromatin, particularly its supposed extrusion through the nuclear membrane. The reasonable probabilities there narrow down to the possibility of nucleolar activity, or to a somewhat intangible, at best ill-defined, coöperation of nucleus with cytoplasm.

With respect to the nucleolar theories the matter obviously turns on whether nucleoli or their products ever traverse the nuclear membrane. To this question endless contradictory answers have been given, but it is significant that those who uphold nucleolar extrusion have not usually stated that they actually saw the essential stages of transfer. Authors who claim, however, to have observed this phenomenon in fixed preparations of gland cells are Ogata ('83), Montgomery ('98), Carlier ('99), Vigier ('00a), Ferrata ('06); refer also to Ludford ('25c). Nucleoli have very often been identified in the cytoplasm on the mere basis of staining capacity. Clearly, such "proofs" are valueless—as much practical experience has shown. Too frequently authors deal with nucleolar migration into the cytoplasm as though it were a "well-known fact," or at most a matter of slight importance. Actually, however, it is exactly this point which is in great present need of being adequately demonstrated or finally disproved. We may hope eventually to get decisive light on this problem through studies which have for their raison d'être exactly the examination of this critical point with no regard for its possible significance. Observation of living cells would be most convincing, even though the conditions of such studies might not be entirely acceptable as normal. On this point, however, very few observations have been made and they would in any event be difficult. Leydig ('88) reported seeing the extrusion of nucleolar derivatives in the egg of *Theridium*, and Ludford ('25c) has recently reported on nucleolar movements in rat fibroblasts grown in tissue cultures, though he was unable to see any actual extrusion of nucleolar material as such. He did, however, observe the appearance of a cytoplasmic vacuole touching the nuclear membrane at its point of internal contact with the nucleolus. He interpreted this as probably

a stage in the extrusion of nucleolar material (see also Dehorne and Hosselet ('28a)). These observations obviously afford a rather tenuous basis for such wholesale nucleolar extrusion as existing accounts in gland-cells require. I think, however, that the extrusion of nucleolar matter may well be a fact in gland-cells, developing eggs, etc., without in any way throwing new light on nucleocytoplasmic interchanges or secretory activity. For during mitosis, the casting out into the cytoplasm of nucleolar material at the close of the prophase is of regular occurrence, although this material has not been shown to do anything beyond gradually merging with the cytoplasm. It seems to me at least conceivable that if the nucleus can thus rid itself of nucleolar material at one phase of its cycle, it might do the same thing at other times when for some reason the nucleolar situation required readjustment. Thus the mere extrusion of nucleolar products during the interphase may be quite devoid of significance so far as the direct origin of secretory materials is concerned. In some such way have Walker and Tozer ('09) viewed nucleolar extrusions, holding that this phenomenon is common to all cells but is particularly emphasized where active metabolic processes are taking place with mitosis occurring only at rare intervals, if at all. Thus the nucleus may adjust itself to the situation by a process which is ordinarily reserved for the mitotic phase, and no more in the one case than in the other is there any reason to suppose that the material cast out has any direct connection with secretory synthesis (see also Jörgensen ('08), Benoit ('26)). Further, a number of authors, while admitting the validity of nucleolar extrusion, have denied that the material thus transferred to the cytoplasm has any visible connection with secretion. On the contrary the extruded nucleoli seem to break up and disappear (Carlier ('96, '99, '05), Petersen ('07), Walker and Embleton ('08)). Montgomery ('98) even thought that the nucleolar material might return again to the nucleus at the close of the secretory cycle. Prenant ('05) and Benoit ('26) frankly consider nucleolar extrusion to be associated with cellular or nuclear degeneration; and nuclear extrusions have indeed been described as unusually abundant in conditions involving pathological degeneration. Refer, for example, to Adami ('06), and Hanitzsch ('13); and also Heidenhain and Werner ('24). To all these sources of doubt must be added the very large number of cases where nucleolar extrusion has not been described as a normal occurrence in gland-cells, and in certain conspicuous instances has been emphatically denied; as, for example, the conclusion of Yamanouchi ('22) on the lepidopteran silk-gland—a classical source of accounts of nucleolar extrusion (refer to page 318)—and the severe criticism of Montgomery's ('98) account of the gland-cell nucleoli in *Piscicola* by Jörgensen ('13), who was unable to find any trace of nucleolar extrusions. So far as the present literature permits any opinion at all, we must accordingly conclude that even if nucleoli are extruded, their exact connection with glandular activity remains in doubt.

The argument for nuclear participation in secretion thus falls back in the end upon indirect evidence such as Korschelt ('89) so cogently urged. The extraordinary nuclear changes which sometimes occur in invertebrate gland-cells are assuredly difficult to account for on any other basis than one of real relationship of some kind with secretory activity. Nevertheless, the stubborn fact remains that in vertebrate gland-cells variations in position shape, size and staining capacity are not

conspicuously exhibited by the nucleus. In many cases the nucleus behaves more as though it had no part in the secretory activities of the cytosome (Bowen, '26d); and Duesberg ('12) concluded that the changes might just as well be explained as evidence of the influence of the cytoplasm on the nucleus, rather than vice versa. M. Heidenhain ('07), indeed, rejected the argument for nuclear coöperation in secretion on the ground that the changes might be equally well interpreted as indicative of "regenerative" operations presumably necessary in cells of such pronounced activity. To my mind, however, the conditions in certain invertebrates can scarcely be so easily dismissed, and it is difficult to avoid the conclusion that these changes really are directly associated with some phase of secretory synthesis.

To conclude, it appears that in general the nucleus has been pretty definitely shown not to be the immediate source of secretions. On the contrary it exhibits much less visible connection with secretory processes than we might have anticipated on a priori grounds. Secretion is a function in which all parts of the cell may very probably be called on for their contribution toward the end-result, and in this process the nucleus seems to do its bit. What this may be in more exact terms, we do not know. Perhaps it is merely a regulative function, or the nucleus may synthesize certain materials required in the cytoplasm for, or as a result of, secretion. Such a conception of nuclear function in secretory activity in terms of some coöperative, as yet intangible, association with the cytoplasm, has indeed been often proposed, recent examples being Lutz ('21), Bowen ('26d), and Tschassownikow ('27). This is admittedly an unsatisfactory and dubious conclusion, but the facts do not warrant anything more definite. Certainly the oft-repeated statements touching on the supposed importance of the nucleus in secretion have a very inadequate and unreliable cytological foundation.

NOTE:—A complete literature list of references from both the first and second sections will be given at the end of the second part.

(To be concluded)

THE INFLUENCE OF THE THYROID GLAND AND HYPOPHYSIS UPON GROWTH AND DEVELOPMENT OF AMPHIBIAN LARVAE

By BENNET M. ALLEN

University of California at Los Angeles

THE amphibians are an unusually favorable group for an investigation of the problem of development from larval to mature form. The transformation from the tadpole to the frog is spectacular, involving rapid deep-seated changes in the entire organism, and there are many criteria by which this process may be measured; as, for instance, the shortening of the intestine, the development of the mouth, the shrinkage and disappearance of the tail, and most significant of all, the development of the limbs. The last named feature gives us the most accurate criterion of all for measuring the degree of development.

The metamorphosis of urodele larvae is not so spectacular, but is none the less significant. B. Zawadowsky ('28) has divided the process of metamorphosis of the axolotl into five stages, during which there is regression of the gills and of the fin folds, protrusion of the eyes, and development of the salamander color pattern. In addition to these criteria, Uhlenhuth has called attention to the fact that the epidermis is shed by urodele larvae often in a single piece at the beginning of metamorphosis, giving the first evidence of that process. He considers the development of the limbs to be of minor significance as indicators of metamorphosis in this group because of their appearance and differentiation in early larval life long before the true evidences of metamorphosis appear as a result of thyroid functioning. This difference in the significance of the limbs as indicators of metamorphosis in the anurans and urodeles is but one of the many points that serve to show that each type, each species, has its own pattern of development; it reacts in its own peculiar fashion to the stimulus that induces metamorphosis.

THE THYROID GLAND

It has long been known that the cretin type of human dwarfism is due to thyroid deficiency, and that this can be remedied by thyroid feeding if administered in time, but it remained for Gudernatsch ('12, '14) to show that the metamorphosis of tadpoles can be enormously hastened by feeding them thyroid material. In his work he used sheep thyroid, but investigations since his time have shown that thyroid glands of any vertebrate can exert this influence when fed.

The most extensive work in the study of the influence of thyroid glands from different types of vertebrates was done by Dr. Horace Gunthorpe at the writer's suggestion. This work is as yet unpublished. It shows that the thyroid glands of all forms of vertebrates studied—fish, whale, sheep, cattle, dog, cat, pig, etc.—can be used to induce metamorpho-

sis, and that each has a specific potency which is not always proportional to its iodine content, as one might assume.

Thyroid feeding is usually soon or later fatal to the tadpole, depending upon the amount administered and the stage of development that the tadpole had previously reached. The larger tadpoles are more readily brought to metamorphosis than those of smaller size. This experiment of inducing amphibian metamorphosis by feeding thyroid material has been repeated innumerable times and is so simple that it can be made a standard experiment in elementary laboratory classes.

Gudernatsch ('12, '14) states that the feeding of thymus glands to tadpoles produces the opposite effect of inhibiting metamorphosis. Swingle, repeating this work with calf thymus, failed to substantiate this phase of Gudernatsch's experiments. Allen ('20) removed the thymus glands of *Rana pipiens* and found that no change in the course of development was produced. Uhlenhuth ('19) showed that feeding thymus material to larvae of *Ambystoma* appeared to retard or prevent metamorphosis only in a few cases when used as the sole food; if mixed with normal food there was no evidence of it—thus leading him to the conclusion that its apparent effect was due to the deficiency of metamorphosis promoting substances in some parts of the thymus substance, not to any retarding influence of that gland.

The action of the thymus gland does not form a part of our subject, and only comes in question here in that it is not found to work in opposition to the thyroid gland, as Gudernatsch claimed.

Effect of removal of thyroid gland

It is desirable in most cases to test out the results of glandular administration, such as feeding or implantation, with experiments in which the gland is removed. Work in this field carried out independently by Allen in 1916 and by E. R. and M. M. Hoskins in the same year, confirmed the results of thyroid feeding in that removal of the thyroid prevents metamorphosis; thus showing clearly that the thyroid gland is normally indispensable to metamorphosis. In these experiments the anlage of the thyroid gland is removed soon after its appearance: at a stage of 5 or 6 mm. total length, in the case of *Rana pipiens*. The operation necessitates the use of a very delicate knife, made from a medium-sized needle by breaking off the eye, inserting the point into a wooden handle, and sharpening to a fine knife edge upon a whetstone. Fig. 1. This must be so well done as to pass muster under a medium power of a binocular microscope. Using an instrument with erect image, the tadpole is laid on its side under water on a paraffin surface and the cut made as shown by dotted line in the diagram. Fig. 2. The removal of the thyroid anlage is then a very simple matter, a little practice making possible the removal of forty per hour. The writer has removed over 250 in one day, with better than 90 per cent success.

In these experiments, the removal of the thyroid gland anlage at its inception gives the clearest possible picture of its rôle in development, because we here have to do with tadpoles in which the gland never has functioned. The absence of the thyroid gland does not affect the rate of growth in size (Allen, '18–'28; Hoskins, '19), nor does it affect the process of early development up to a definite stage that differs in different species. In *Rana pipiens* development ceases at a period shortly after the appearance of the hind limb buds and before they reach a length

of 1 mm. Up to this stage in normal tadpoles there is no accumulation of colloid in the thyroid glands in *Rana pipiens*, and as a consequence, these remain small.

In *Ambystoma microstomum* both fore and hind limbs begin to grow before any colloid is formed in the thyroid gland. In *Bufo americanum* it appears almost immediately after the hind limbs have begun to grow, while in *Rana pipiens* it appears practically simultaneously with the anlage of the hind limbs (Allen, '18). In *Bufo americanum* the hind legs continue growing until they soon reach a length of 1.5 mm. at the stage when the operated tadpoles begin to show limb growth different from that of the controls. The leg length in *Bufo* is more significant than at first appears, because the tadpoles of *Bufo* are much smaller than those of *Rana*, and the relative difference in development of the limbs is thus accentuated. The tadpoles of *Bufo* continue to grow, attaining a length of trunk over twice that attained at the stage of development arrest. In these giants the hind limbs may reach a length of 7 or 8 mm. and an increased degree of differentiation. This is in contrast to the condition of *Rana pipiens*, where growth of the hind limbs little exceeds the general proportions to body size at the stage of development arrest and where there is no evidence of continued differentiation (Allen, '25).

It might be argued that during these earlier stages there is such slow secretion that the colloid is used up as rapidly as it is formed. This seems to be disproven by the fact that thyroidectomized tadpoles reach this stage as soon as do the normal tadpoles. It is possible that the slight accumulations of colloid in young tadpoles might not contain the essential substance of the secretion thyroxin at this time. No determinations regarding potency of the earliest colloid of tadpoles have yet been made. Administration of the thyroid glands of young pig embryos shows that they are capable of inducing metamorphosis at the earliest stages at which colloid appears in the follicles (Hogben and Crew, '23).

From this point on, the difference in development between thyroidectomized and normal tadpoles is most striking. The former continue to grow in size and the development of internal organs and

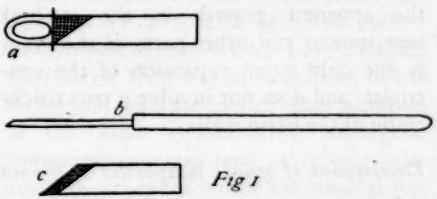

FIG. 1. METHOD OF MAKING THE KNIFE FOR PERFORMING OPERATIONS UPON TADPOLES

a, Breaking off the eye of the needle. *b*, The knife mounted in its handle. *c*, The cutting edge.

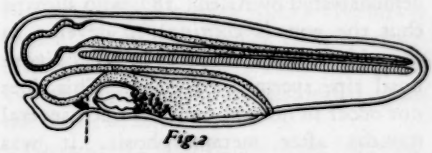

FIG. 2. DIAGRAM OF SAGITTAL SECTION OF TADPOLE TO INDICATE POSITION OF THYROID GLAND ANLAGE, SHOWN IN SOLID BLACK, AND PLANE OF CUT AS SHOWN BY THE DOTTED LINE

external features proceeds in the absence of thyroid secretion to a definite stage, beyond which further development is possible only in response to the stimulus given by the administration of iodine or some of its compounds or by thyroid implantation. In normal tadpoles the thyroid secretion accumulates very rapidly after the gland becomes active and the development toward metamorphosis keeps pace with its increase in size (Allen, '19).

The extirpation of the thyroid gland not

only inhibits development toward maturity in external features of body form, but equally affects all other somatic characters studied, even the internal organs: as, tongue, intestine, stomach, pancreas, persistence of pronephros, bladder, ossification of the bones (Terry, '18), and brain development (Allen, '18). Hoskins ('19) claimed that the brain continues to develop to an appreciable degree in the absence of the thyroid gland. This was contested by Allen ('24) who claimed, upon the basis of a study of transverse sections, that the apparent growth in the cerebral hemispheres and other parts of the brain is due only to an expansion of the ventricles, and does not involve a true thickening of the brain walls.

Development of gonads independent of thyroid

In contrast to the complete dependence of the development of the somatic structures upon the thyroid gland, is the independence of the gonads. This was demonstrated by Allen ('18), who showed that the gonads continue to develop in thyroidectomized tadpoles of *Rana pipiens* until ripe sperm are formed. This does not occur in normal tadpoles until several months after metamorphosis. It was similarly shown that the ovaries and the contained oocytes develop to a size far beyond that reached at metamorphosis. Hoskins ('19) made substantially the same observations in thyroidectomized *Rana sylvatica*. Swingle ('18) showed the converse of this: namely, that feeding thyroid preparations to tadpoles does not accelerate the development of the germ cells or germ glands. This development of the gonads independently of the soma is in line with the well known case of the axolotl in nature and many other cases of paedogenesis.

In this connection we might well consider the interesting investigations of several workers who have shown that different organs or sets of organs have different thresholds of response to thyroid stimulation, or that there may be organs that are wholly unaffected by it. Uhlenhuth ('21) contends that the limbs of larval salamanders are not under the control of the thyroid gland, and states that when iodothyrine is fed to the larvae of *Ambystoma opacum* at a sufficiently early stage rapid metamorphosis of the body is induced without affecting the limbs; resulting in the production of a salamander with poorly developed hind limbs, which may not have the full number of toes. Conversely he claimed that he was able to inhibit metamorphosis of this salamander by feeding thymus preparation—iodine-deficient food—without, however, affecting the development of the limbs, which grew out of proportion to the body as a whole. Blacher ('28) has done a most interesting and suggestive piece of work along this line. He studied the threshold of stimulation necessary to induce development of different features in the tadpole as measured by different dilutions of thyroidin. The tadpoles were immersed in a given solution for three days; at the end of which time they were killed and measurements taken. He found that the intestine responded to as weak a solution as 0.002 per cent. Twice this concentration was required to stimulate the growth of the tail. Growth of the trunk, the shedding of the horny larval jaws, and the emergence of the fore-limbs required twenty-five times the amount necessary to induce growth of the intestine. When the concentration rises above a given optimum point, stronger concentrations do not produce as great a response as does the optimum strength. Blacher considers the objection that certain processes might respond less quickly and less readily because of their complex

character; the emergence of the fore-limbs being an example. He holds that there is a true difference in the threshold of stimulation aside from the differences in the complexity of the parts involved.

Uhlenhuth ('19) attacks the view tentatively advanced by the writer (Allen, '18), regarding the significance of continued development of the gonads of thyroidectomized tadpoles after further differentiation of the somatic structures has been inhibited as indicated above. He states,

> Development of the skin coloration, as well as development of the legs, sex organs, tongue, and palatal teeth are all caused by substances not identical with the substances causing metamorphosis, and since they are all independent of each other in their development, it is probable that special chemical mechanisms exist for the development of each one of these six groups.

A review of this character is not the occasion for a lengthy controversy upon points of difference. The writer would be the last one to contend that development is a rigid process from which there may not be deviations in the case of individual organs. There must be many factors at work, internal and external, and it is quite reasonable to suppose that the different structures may have different thresholds of response to stimuli. Certain structures like the legs of urodeles appear early in development and are not affected by metamorphosis as they are in the anurans. Each species certainly has its own peculiar pattern of response to the stimulus of the thyroid gland. In spite of all this, it does seem to the writer significant that the gonads in both urodeles and anurans develop to a high degree, even to sexual maturity, while the body as a whole remains in its larval condition. This is especially significant in the case of the removal of the thyroid gland—one single factor—which brings about such a sharp distinction between soma and germinal tissue while all the external factors are uniform.

Effect of thyroid on non-metamorphosing amphibians

Reference has already been made to the fact that different types of amphibians react in different degree to the influence of the thyroid gland. It may be well for the sake of our readers who are not zoologists to explain that axolotls, of which mention has been made above, are members of a species of salamander—*Amblystoma tigrinum*—that have retained their larval form and aquatic habit of life far beyond the period when other members of the same species have undergone metamorphosis into land inhabiting salamanders—in other words the axolotl has failed to metamorphose as regards all of its somatic characteristics and yet has become sexually mature. Such cases occur in certain regions such as the plateau of Mexico, and our own Rocky Mountain region of Colorado. The Colorado axolotls transform more readily when removed from their natural habitat than do the Mexican forms.

Necturus, the mud-puppy of the lakes and streams of the Mississippi Valley, is classified as a Perennibranchiate because it retains its gills and full larval character throughout life. It is naturally of interest to study the thyroid glands of these forms and to determine by experiment whether metamorphosis into a salamander form is possible.

In a brief abstract the writer (Allen, '18) showed that the thyroid gland of the Colorado axolotl is of much the same structure and of equal size with that of the normal metamorphosed form of the same species, and that colloid is present to the same degree in both. Swingle ('22) demonstrated that the thyroid glands

of the Colorado axolotl are capable of inducing metamorphosis in other forms. He cut up the thyroid glands of a single axolotl, *Amblystoma tigrinum*, into six pieces, and implanted them into immature larvae of *Rana clamata*, causing five of the latter to undergo metamorphosis.

In 1918 the writer carried out unpublished experiments in feeding Armour's powdered thyroid gland substance to adult Necturus, but failed to produce any tendency toward metamorphosis. Swingle ('22) repeated this experiment, likewise without result. It remained for Gutman ('26) to attain a slight measure of success in this line by immersing young Necturus 37 mm. in length in dilute solutions of thyroxin, the essential secretion of the thyroid gland. This alone produced no results, but was effective when used in conjunction with adrenalin. There was advanced reduction of the gills and distinct exopthalmos with change in the form of the head. The larvae invariably died before undergoing any complete metamorphosis. Further work along these lines must prove extremely interesting. Swingle ('22) demonstrated the fact that the thyroid gland of Necturus is capable of producing an active secretion by transplanting $\frac{1}{4}$ the thyroid substance of an adult Necturus into an immature larva of *Rana clamata*, thereby greatly hastening metamorphosis.

Is this failure to metamorphose even when large quantities of the active thyroid secretion have been elaborated and stored up by the animal's own glands due to an inability of the tissues of the animal to respond to the stimulus of the secretion or is it due to the absence of a "releasing mechanism" as claimed by Uhlenhuth ('19)?

Swingle ('24) removed the thyroid glands from Colorado axolotls 7.5 inches long, broke them up, and injected the contents intraperitoneally into the individuals from which they were removed. Two months later there were no evidences of metamorphosis. In a later series, two sets of thyroid glands were injected into each animal; likewise without results. This procedure may not constitute a fair test, because absorption through the peritoneum may not be equivalent to that through the blood stream. Assuming that the procedure affords a fair test, the conclusion would be that we do not have here a failure to respond to a "releasing mechanism" as stated by Uhlenhuth ('19) etc., but a failure on the part of the axolotl to respond to its stored thyroid secretion—sufficient, as shown above, to induce metamorphosis in several tadpoles of other species, as Swingle ('22) demonstrated.

The process of thyroid secretion

While it is not within the scope of this review to enter into an exhaustive discussion of the process of secretion in the thyroid gland, a brief survey will help to a clearer understanding of our problem. The most comprehensive studies of the secretory activities of the thyroid glands of amphibians have been made upon salamanders by Uhlenhuth ('27, '28), who bases his results upon studies both of fixed and of fresh material stained with intra-vital stains. The gelatinous secretion "colloid" is stored in the follicles and discharged from them through the investing layer of secretory cells into the surrounding blood vessels. Uhlenhuth ('27) finds that the secretion is first seen in the cells in the form of small granules that unite into larger droplets. These are of two kinds: chromophobe and chromophile, both of which are discharged into the lumen of the follicle, there to be consolidated into the colloid mass. The chromophile secretion appears as acidophile droplets that accumulate in the

apical ends of the secretory cells directed toward the cavity of the follicle. They diffuse into the follicular cavity and after a time change to a basophile condition. The chromophobe secretion is produced in the basal part of the cell, and collects in the intracellular (Anderson) vacuoles, migrates to the apical pole, and passes into the cavity, where it collects to form the "colloid vacuoles" which Uhlenhuth considers to be an essential element of the thyroid secretion. He traces the passage of the secretion through pores between the epithelial cells of the follicles.

According to Uhlenhuth there is a gradual production of thyroid secretion during larval life, becoming more active shortly before metamorphosis and in periods of adult life. These periods of activity are characterized by a decided thickening of the secretory cells, which become columnar in section. They also show increased numbers of secretion granules. The discharge of the secretion results in a sudden decrease in the colloid content of the follicles. After such a discharge there follows renewed activity in colloid secretion. The production of secretion and its discharge into the follicle is continually taking place, and is an elementary function of the thyroid gland. The discharge only occurs in response to external stimuli which are imparted by a special discharge mechanism. In another paper Uhlenhuth ('27) states his view that the anterior lobe of the hypophysis performs the function of a discharge or releasing organ, enabling the thyroid gland to throw its load of secretion into the blood stream. We shall discuss this point in a later portion of this paper.

Huxley ('20) demonstrated the possibility of inducing metamorphosis in the axolotl by feeding it thyroid preparations. We must keep in mind the fact that its own thyroid glands have the potency demonstrated by Swingle and yet do not induce any tendency toward metamorphosis during the years that the axolotl may remain in its larval condition. This, together with the fact that Swingle ('24) failed to induce metamorphosis by injecting the axolotls' own crushed glands even in double dose, would lead us to infer that the axolotl is only able to respond to thyroid secretion superior to its own either in quantity or quality.

Is the thyroid influence exerted directly or through the nervous system?

Some interesting studies have been made upon the question of whether the thyroid influence is exerted directly or through the medium of the nervous system or other surrounding factors. Huxley ('25) kept half-grown larvae of *Rana temporaria* that had been fed with fresh ox thyroid, in solutions of urethane, where they remained thoroughly narcotized for eight or ten days. The process of metamorphosis proceeded at the same rate as in similarly fed tadpoles that were not kept in a state of narcosis. This experiment was varied by keeping them in solutions made from thyroid tablets, but the results were the same. He also performed experiments of a different nature where metabolism was directly affected. Potassium cyanide in weak solution had a retarding effect upon metamorphosis of tadpoles to which thyroid material was fed. Huxley produced the same interference by subjecting the containers in which the tadpoles were kept to an atmosphere of oxygen. This treatment probably does not involve the nervous system at all but acts directly to lower the responsiveness of the tissues. This at least could be easily understood in the case of the potassium cyanide treatment. These results found verification in the later work of Spaul ('28), who extended the experi-

ments to deal with the influence of the hypophysis; which we shall consider later in its proper place. One interesting feature of his work in this connection is his demonstration that the metamorphosis of thyroid-fed tadpoles is retarded by subjecting them to the influence of X-rays.

Returning to the more crucial question of the relation of the developing organs to their surroundings—and the nervous system—we may refer to the work of Helff ('27), who made autoplastic transplantations of the tongue to the back of normal tadpoles. Muscles, glands, and papillae developed in normal fashion in spite of the abnormal position and innervation. The writer can testify that the tongue remains in a rudimentary condition in thyroidectomized tadpoles. We are quite ready to accept Dr. Helff's interpretation that its differentiation is controlled by the thyroid hormones. An interesting addition to this experiment would be the transplantation of the tongue from normal tadpoles to the backs of thyroidectomized individuals.

Iodine as a constituent of the thyroid secretion

It has long been known that iodine is the most essential element in the thyroid secretion. The thyroid gland is the only organ in the body that contains any considerable amount of it. Marine and Rogoff ('16) showed that when iodine is injected into an animal it is fixed by the thyroid gland in a few minutes. Efforts to isolate the essential thyroid secretion have been numerous. Baumann ('95, '96) isolated iodothyrin, which contains the active substance, but not in a pure form. Investigations by Kendall ('14, '17, '19) and later by Harington ('26) showed the pure form of the active secretion of the thyroid gland to be a substance which Kendall named thyroxin. Regarding the exact chemical formula for thyroxin, there is some difference of opinion between Kendall and Harington; the former giving it as $C_{11}H_{10}O_3NI_3$ with one benzine ring, and the latter making it $C_{15}H_{11}O_4NI_4$ with two benzine rings. It is not within the scope of this article to go into questions of biochemistry, but we shall hope to touch upon some of the more significant experiments upon the influence of this and other iodine compounds upon amphibian development. Morse ('14) experimented with various iodine compounds which he applied to tadpoles in an effort to determine the active substance of the thyroid secretion. He immersed tadpoles in solutions of iodine, potassium iodide, iodobenzoic acid, iodoxy-benzoic acid, without producing any tendency toward metamorphosis. Strangely enough, he fed them starch iodide without producing any symptoms of metamorphosis. This is quite similar to the method first successfully applied by Swingle. It is hard to account for Morse's failure, unless he may not have allowed a sufficient length of time. Immersion in solutions of iodine salts is slow in inducing metamorphosis.

Swingle ('18) brought about the metamorphosis of *Rana pipiens* by feeding tadpoles a mixture of iodine and flour. The iodine enters into a very loose association with the starch of the flour, and we get the effect of pure iodine. This was eaten by the tadpoles in quantities vastly greater than met with in normal food and water. Metamorphosis occurred in much the same fashion and in about the same length of time as produced by thyroid feeding. We might assume that the tadpoles had used this rich supply of iodine to synthesize thyroxin by means of their immature thyroid glands, but this explanation was disproven by Swingle's work in feeding the same food to thyroidectomized tadpoles and attaining the same results. At the same time the writer

(Allen, '19) fed the iodine and flour mixture to Rana and Bufo tadpoles that had been hypophysectomized and to those from which both the hypophysis and thyroid gland had been removed. It will be shown later that the presence of both the thyroid gland and the anterior lobe of the hypophysis is essential to metamorphosis under normal conditions of food and water. Yet with relatively large doses of iodine, the tadpole is able to undergo metamorphosis without them. One can only conjecture whether the various tissues of the body are capable of directly using the inorganic iodine or whether certain organs may take over the rôle normally played by these endocrine glands. We thus conclude that so far as metamorphosis is concerned, one of the functions of these two glands is to enable the tadpole to make use of the minute quantities of iodine that occur in the normal environment.

The function of the thyroid glands in this connection is well illustrated by Swingle's ('19) finding that metamorphosis of normal Rana larvae could be induced by a concentration of iodine below 0.0000003833 per cent—the weakest used in his experiments, but double this concentration was insufficient to induce metamorphosis in thyroidectomized tadpoles even when they were exposed to it for fairly long periods of time.

Between iodine and thyroxin is a great gap, and many experiments have been performed upon iodine compounds of intermediate degrees of complexity; but it is not always easy to evaluate these findings because of the various means of administration; such as feeding, peritoneal implantation, injection, and immersion in weak solutions, so the results are far from possessing quantitative value. At the same time, it is well to note that Swingle ('19) found a marked difference in the effects of certain simple inorganic iodine compounds. Iodine alone was most potent, while next in order were iodoform and potassium iodide. Potassium iodate was eaten by the tadpoles, but did not cause metamorphosis in Swingle's experiments. He considers this to be due to an inability of the tadpole to break down the molecule and release the iodine.

Passing to the more complicated substances, Morse ('14) stated (page 426) "It is clear that the iodine-bearing portions of the thyroid substance, that is, thyreoglobulin and iodothyrin, give results which can not be distinguished from those obtained by feeding the desiccated powder or tablets." He also showed at the same time that 3–5 di-iodo-tyrosine induces metamorphosis, but not as readily as intact thyroid substance.

Abderhalden and Schiffmann ('22) verified this last point and likewise showed that di-iodo-tyramine and several other substances of character similar to these likewise induce metamorphosis. They failed to attain this result by feeding iodo-acetyl di-iodo-tyrosine, B-iodo-propionic acid, and tyrosine. Romeis ('22) also induced metamorphosis in tadpoles by the use of di-iodo-tyrosine, but found that it was not as active as thyroxin.

Abelin ('21) made extensive studies on the influence of inorganic and organic iodine compounds; among the latter being tyrosine and di-iodo-tyrosine. His work showed that iodine is the essential constituent of these substances in inducing metamorphosis.

These results with tyrosine and di-iodo-tyrosine were verified by Swingle ('22), who induced metamorphosis in thyroidectomized and hypophysectomized larvae of *R. sylvatica* by feeding di-iodo-tyrosine. He then proceeded to demonstrate in clear fashion the significance of iodine in its association with amino-acids

by feeding pure tyrosine to one set of tadpoles, 3–5 di-iodo-tyrosine to a second set, and 3–5 di-brom-tyrosine to a third set. In this series only the combination containing iodine was shown to induce metamorphosis. Bromine, although akin to iodine, was thus shown to have no effect when it was used to replace the iodine, and administered under identical conditions.

Kendall ('19) showed that acetylated thyroxin had lost its power of affecting basal metabolism when applied to mammals, but that it had lost none of its capacity for inducing metamorphosis in amphibians. Swingle, Helff, and Zwemer ('24) repeated and extended this work, fully substantiating the findings of Kendall.

Gayda ('22), feeding and injecting thyroid gland material of warm-blooded animals into such cold-blooded forms as frogs, caused only slight heat production. Oxygen consumption, on the other hand, was shown by Huxley ('25) to be increased 100 per cent in larvae of *Rana temporaria* as a result of exposure to moderately strong thyroid solutions for periods of four to six days.

M. M. Hoskins ('27) has given good evidence to show that acetylated thyroxin accelerates development of new-born rats, when injected hypodermically. It will be of much interest to further extend these experiments upon young mammals to determine whether the element iodine or its simpler compounds can produce modifications of early development comparable to the influence that they exert upon amphibian metamorphosis.

We may well accept the conclusion that this effect is quite different from the metabolic stimulus that can only be exerted by the unmodified thyroxin. There has been, in general, a tendency among investigators to emphasize the differences in the influence of iodine and its compounds upon amphibians and upon mammals. Color is given to such a view by the great differences in the readiness with which the reaction to iodine and its derivatives is shown within the amphibian group itself when we compare its effect in the anurans and the urodeles.

Since Swingle's demonstration ('18) no one has seriously contested the finding that inorganic iodine—even the element iodine—can induce metamorphosis of anuran tadpoles when administered in food, when injected, or when mixed in the water in which they live. There is also universal agreement that metamorphosis of urodele larvae can be induced by thyroid feeding, immersion in, or injection of thyroxin, iodothyrine, etc., but Uhlenhuth ('21) as a result of studies upon *Ambystoma*, claims that inorganic iodine has no effect upon Salamander metamorphosis. This is in line with the thesis maintained by Uhlenhuth to the effect that the process of manufacture and storage of thyroid secretion does not insure its release, which can come only through the agency of a releasing mechanism, with which the administration of inorganic iodine has nothing to do.

On the other hand, Huxley and Hogben ('22) metamorphosed Salamander and Triton larvae by immersion in dilute solutions of iodine. In the case of *Necturus* and other urodeles, it is much more difficult to induce metamorphosis by means of inorganic iodine, and efforts have been made to accomplish this by immersion in solutions and injection of solutions, but they have failed to attain results. Huxley and Hogben ('22) fed iodine to the Axolotl, but failed to cause it to show any signs of metamorphosis. Later Huxley ('25) repeated the feeding experiments and in addition kept axolotls in iodine solutions, but only succeeded in inducing

some of the changes associated with the early stages of metamorphosis.

Success in inducing metamorphosis of the axolotl by means of inorganic iodine has been attained by Abelin ('21) Hirschler ('22), Blacher and Belkin ('27) and by Zawadowsky, Raspopowa, Rolitsch, and Umanowa-Zawadowskaja ('28). The last named group of investigators attempted to induce metamorphosis of this form by immersion in iodine and Lugol solutions, and by injection intraperitoneally, but this treatment has given only equivocal results. Hirschler was successful through peritoneal implantation of a crystal of iodine encased in cotton and collodion. This method was modified by Blacher and Belkin, who wrapped the iodine crystal in a thin sheet of cotton moistened with salt solution. B. M. Zawadowsky and his associates successfully repeated this experiment, employing the method of Blacher and Belkin. Ingram ('28) induced metamorphosis in thyroidectomized and hypophysectomized Colorado axolotls by the subcutaneous implantation of iodine crystals.

It is thus clear, so far as the experiments go, that all amphibians which are known to metamorphose under any circumstances can be induced to do so by the proper application of inorganic iodine. In the urodeles, this is far more difficult than in the anurans, and is especially difficult in the neotenous axolotl, where the strongest and most direct application of iodine crystals is necessary.

The administration of organic iodine results in an increase in the amount and density of the colloid secretion in the thyroid follicles. This was shown in amphibians by Swingle ('19) in his work upon *Rana pipiens*. It had been previously demonstrated by Marine and Williams ('08) and by Marine and Lenhart ('09) in man, the dog, and sheep, ox, pig, cat, and fish. The amount of stainable colloid was clearly shown to vary with the amount of iodine available. In fact, these workers have explained the effect of iodine in the treatment of goiter upon the principle that it induces an increase in the amount of colloid stored in the thyroid follicles and that this in turn brings about an involution of the hypertrophied and hyperplastic secretory epithelium.

The effect of goitrous thyroids

While it is far from the purpose of this paper to discuss the goiter problem, we cannot resist the temptation to discuss several papers upon this subject that serve to illustrate the principles of amphibian development. There is indeed a widespread tendency to use tadpoles in biological tests to determine the functional activity of pathological thyroid glands. This type of work is of interest to the biologist not only for the light that it throws upon our problems, but because it tends to demonstrate the practical value of our work.

Among the earlier papers in this field is that of Lenhart ('15), who fed to tadpoles human thyroid glands taken from different types of goiter, simple and exophthalmic types. All produced metamorphosis. Graham ('16) fed tadpoles with material from pathological human thyroid glands and showed that preparations of thyroid gland from adenomatous goiter cases induced metamorphosis but not so readily as does material from normal thyroids. In either case, the influence is exerted by active iodine content. Abderhalden and Schiffmann ('22) performed similar experiments with normal and goiter affected glands, and likewise came to the conclusion that both induced metamorphosis, the speed being directly proportional to the iodine content.

Abelin ('27) fed tadpoles with thyroid

glands affected with various forms of goiter and also administered glands of human and calf embryos. In all of this work he took the iodine content into account and observed a uniform method of feeding the tadpoles. Of the five cattle embryos used, only one had visible colloid in the follicles; four of them, however, contained an appreciable amount of iodine and induced metamorphosis in tadpoles to which they were fed. He concluded that there is no necessary correspondence between colloid content and capacity to induce tadpole metamorphosis, between colloid content and iodine content, nor between iodine content and capacity to induce metamorphosis. He concluded that the active thyroid substance does not first develop as colloid in the follicle cavities, although it is stored there, and that the iodine is not all present in a chemically active combination.

The work of Tatum ('19, '20) developed a clever method of separating the colloid contents from the cellular material of mammalian thyroid glands. He found that iodine occurs both in the cells and in the colloid secretion, mostly, however, in the latter. This determination was made in beef, sheep, and pig thyroid glands. Studies upon the dog failed to demonstrate such quantities of iodine in the cell tissues. Van Dyke ('21) found that there is a constancy in the iodine ratio of the colloid as compared with tissues in the thyroid gland of the dog and man in spite of decided morphological variation.

Cooksey and Rosenblatt ('28) came to very similar results. They likewise found that the effect of pathological thyroid glands upon metamorphosis is not proportional to the iodine content, thus leading us to conclude that much of the iodine stored in the thyroid gland is not in the form of an active substance (thyroxin). They concluded (p. 13):

> Feeding experiments were conducted in which various types of goitrous glands from human beings were fed to tadpole larvae. There is evidence from these experiments that thyroid glands from clinically active cases of goiter actually contain more active thyroid principle per unit weight than the normal thyroid. Other goitrous glands contain less active principle by this biologic test, and the amounts were directly proportional to the clinical activity of the patient. Old non-toxic adenomas contained less active principle per unit weight than normal, while one gland which had had much roentgen-ray treatment and rest also contained less active principle per unit of weight.

These investigations are in line with the unpublished work of Gunthorpe, in which he showed that administration of the normal thyroid glands of different types of vertebrates exerts an influence that is not necessarily proportional to the iodine content.

There is not the slightest doubt that the form in which iodine is combined by the thyroid gland plays a very important rôle in determining its activity. Thus far thyroxin from mammalian thyroid glands has been chemically isolated as the active substance. It is quite possible that other types of vertebrates may form other iodine compounds of similar nature but with potency different from that of thyroxin, and it is possible that there are quantities of iodine held in storage but not formed into thyroxin. It had been fully demonstrated that the functioning of the thyroid gland depends upon the available store of iodine, and we should very naturally suppose that factors influencing the organism as a whole should affect the activity of the thyroid gland in utilizing the iodine that it receives. Adler ('16) made a histological study of the thyroid glands of tadpoles reared under different climatic conditions. Those from the Alps show large thyroid glands with small follicles, while specimens from the coast of the Adriatic have small thyroids

containing a few large vesicles, and those taken in middle Germany have thyroids of intermediate character corresponding to the climatic conditions. Tadpoles kept at a high temperature are retarded in their metamorphosis and to a lesser degree in growth, the result being abnormally large size at metamorphosis. If the temperature change be from low to high—10°C. to 30°C.—growth is retarded more than the process of metamorphosis, resulting in a smaller size at metamorphosis. On the other hand, a change from high to low temperature results in a larger size at metamorphosis. Terini ('19) found that a temperature of 28°C. applied to thyroid fed tadpoles caused great acceleration in their metamorphosis as compared with thyroid fed tadpoles at a temperature of 9°–15°C. He pointed out the well established fact that high temperature alone does not cause asymmetrical development, although the administration of thyroid material as food does.

Do the tissues store thyroxin?

Some attention has been given by various authors to the question of continuance of metamorphosis after discontinuance of an initial stimulus. Most observations along this line have been incidental to other lines of investigation and have concerned the discontinuance of thyroid feeding. Investigations of this kind should be tested by careful investigation of the contents of the alimentary tract. A very clever experiment was performed by M. M. Hoskins ('22) in which she removed the thyroid gland of the tadpole and implanted it into the tail. When the tadpoles thus treated had reached maximum size and had well developed legs, she cut off the tail with the implanted gland. In most cases the tadpole completed metamorphosis in response to the initial stimulus.

Abderhalden and Wertheimer ('28) have made an interesting investigation of the capacity of the different tissues to absorb thyroxin from a solution in which they are placed. This problem was attacked in two ways: (1) by feeding to tadpoles various tissues such as liver, muscle, blood corpuscles, etc., that had been soaked in thyroxin solutions; (2) by the reciprocal method of observing the amount of thyroxin removed as determined by placing tadpoles in the solutions into which the tissues had been immersed. In all cases it was shown that muscle tissue has the greatest affinity of all for thyroxin. The muscle absorbs the thyroxin within half an hour, longer immersion causing no further absorption. The thyroxin cannot be boiled, soaked or compressed out of the tissues.

Kahn ('24) fed tadpoles with the tissues of tadpoles that had been stimulated to metamorphosis through thyroid feeding. Such tissues did not induce metamorphosis, showing that they had not stored any considerable part of the thyroid substance fed.

Zavadovsky and Novikov ('26) studied the rôle of the different components of the blood in transporting thyroxin, their results being in line with the later observations of Abderhalden and Wertheimer ('28) mentioned above as regards the erythrocytes. After these had been soaked in thyroxin and later washed, they were incapable of inducing metamorphosis of axolotls into which they were injected. The serum, on the other hand, plays a dominant rôle in carrying thyroxin.

It does not come within the scope of this paper to discuss the influence of the thyroid gland or its derivatives upon invertebrate forms. In general, we may say that the evidence from many investigations upon a great variety of invertebrates themselves possessing no

thyroid gland shows that they are not capable of responding to its influence by changes in the nature of metamorphosis or hastened development. Evidence of this among vertebrates outside of the amphibians is scanty indeed, but this is an important field of investigation where a proper comparison can be established between metamorphosis and differentiation.

Ukita ('19) studied the effects of thyroidectomy of pregnant rabbits upon the growth and development of the foetus. He showed that there is great prolongation of the period of gestation and that the young at birth are weak and show incomplete ossification. Their thyroid glands have undergone hypertrophy, and abnormalities are produced in the post natal growth of the bones. These deficiencies are in line with the findings in many cases of cretinism.

The metamorphosis of tadpoles and the process of development in mammals certainly must be essentially comparable, but mammalian differentiation is by no means so spectacular as metamorphosis. We have every reason to hope that experiments upon the influence of the thyroid gland in mammalian embryonic development may prove to be of great theoretical and practical importance; but up to the present time very little indeed has been done in this field.

THE ANTERIOR LOBE OF THE HYPOPHYSIS

In the hypophysis or pituitary gland we have to do with a complex of four different glands that are functionally distinct from one another so far as our knowledge justifies an opinion. The illustration, Fig. 4, indicates these parts and shows their relation to one another. We shall not attempt to discuss the use of the terms hypophysis and pituitary, but shall distinguish them as pars anterior, pars intermedia, pars tuberalis and pars nervosa of the hypophysis. The older accounts distinguished only two portions: the anterior lobe, which corresponds to that part as at present recognized, and the posterior lobe, which corresponds to the pars intermedia and pars nervosa. The pars tuberalis was the last discovered, and has only recently been taken into account. We know very little, if anything, of its function, although it should be possible though difficult to carry out experiments along this line. It is no doubt known to most of our readers that this complex of glands lies under the very center of the brain, occupying in the mammals a deep socket called the sella turcica that constitutes an important landmark in the center of the floor of the brain case.

For many years the hypophysis was known only because it occupies this landmark, not because of any functional significance that was ascribed to it; but the endocrine investigations of recent years have shown it to exert a profound influence upon the body.

Embryonic development of the hypophysis

Before we lose sight of the different divisions of this gland complex, we must take account of the embryonic development. Pars anterior, pars intermedia, and pars tuberalis all develop out of the same anlage growing inward from the surface ectoderm. In the mammals this ingrowth arises from the roof of the mouth and is termed Rathke's pocket, while in the amphibians that concern us here, it arises as a solid tongue of cells growing horizontally inward from the surface ectoderm above the anlage of the mouth. It extends to the infundibulum. After a time it breaks away from the surface ectoderm and differentiates into the anterior, intermediate and pars tuberalis portions of the hypophysis. The

pars nervosa, on the contrary, arises from the tip of the infundibulum.

Effect of removal of hypophysis

One of the first methods of attacking an endocrine problem is to study the effects produced by a removal of the gland in question. The earliest work of hypophysectomy performed upon tadpoles was that of Adler ('14). His method was to burn out the gland by applying an electric cautery to the roof of the mouth of the 20 mm. Rana tadpoles. This operation resulted in a very high degree of mortality, and he was able to rear only three specimens out of many hundreds operated. As a result of this operation metamorphosis was prevented—the hind limbs persisting as mere buds many months after the control tadpoles had metamorphosed. Adler also noted that the absence of the hypophysis exerted a profound influence upon the thyroid gland, which was markedly retarded in growth and contained only a small amount of colloid of fluid consistency.

A different method was simultaneously devised by Allen and by Smith in 1916. E. R. Hoskins, B. M. Allen, and P. E. Smith independently contrived a method of removing the anlagen of endocrine glands by cutting them out at their first appearance. Hoskins in New York City operated upon the thyroid gland, Smith in Berkeley, California, removed the hypophysis, and Allen, in Lawrence, Kansas, removed both; each without any knowledge of the work done by the others. Smith and Allen made reports upon their work at the San Diego meeting of the Western Society of Naturalists, August 9–12, 1916. The printed report of Smith's work appeared in *Science*, August 25, '16, and Allen's account appeared in *Science*, November 24, '16. While our method of attacking these problems has been the same, our interests have been along somewhat diverse lines, but where they have converged, we have usually found ourselves in substantial agreement.

This method of removing the buccal anlage of the hypophysis entails little mortality, and has the added advantage of depriving the animal of the gland anlage without leaving a trace and of assuring that we are dealing with animals in which the gland never has functioned to the slightest degree. The operation is performed as shown in figure 3 at the period when the tail bud is first appearing—3.5 mm. to 4 mm. total length in *Rana pipiens*. The wound heals in a short time, and the tadpoles show no serious defects save for an occasional specimen in which the mouth is defective. These specimens can readily be detected and eliminated. The results that we shall discuss are shown to be due to the absence of the glands, and not to the trauma of the operation, as seen by comparison with normal control specimens that had been cut in the same manner and the gland anlage left untouched.

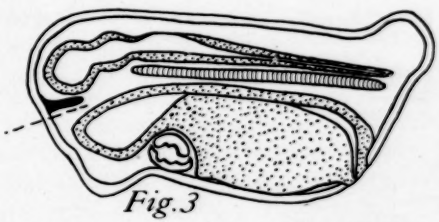

FIG. 3. DIAGRAM OF SAGITTAL SECTION OF TADPOLE TO INDICATE POSITION OF BUCCAL ANLAGE OF THE HYPOPHYSIS, SHOWN IN SOLID BLACK, AND PLANE OF CUT AS SHOWN BY THE DOTTED LINE

It will be recalled that the buccal anlage thus removed is the source from which the pars anterior, pars intermedia, and pars tuberalis develop (figs. 4 and 5). When we use the word "hypophysectomy" we have reference only to the buccal

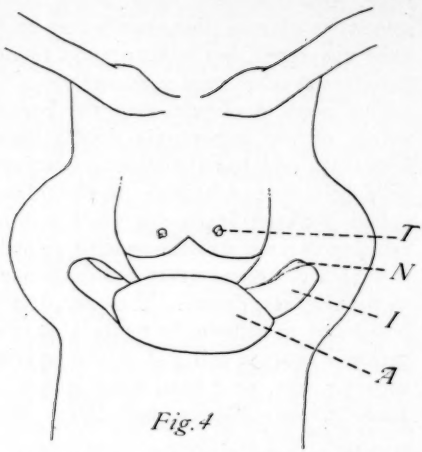

Fig. 4

FIG. 4. UNDER SURFACE OF THE BRAIN OF THE ADULT RANA AURORA DRAYTONI SHOWING THE FOUR PORTIONS OF THE HYPOPHYSIS IN SITU

A-Pars anterior; *I*-Pars Intermedia; *N*-Pars Nervosa; *T*-Pars Tuberalis.

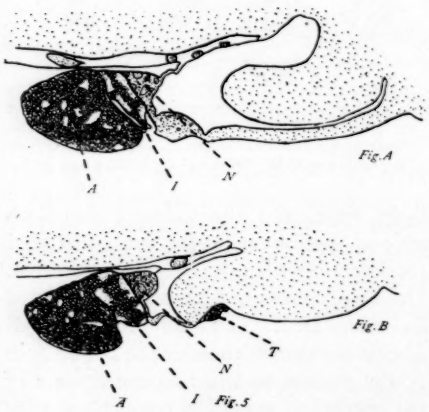

FIG. 5. FIG. 5*a* REPRESENTS A MEDIAN SAGITTAL SECTION OF THE HYPOPHYSIS OF RANA AURORA DRAYTONI. *A*-PARS ANTERIOR; *I*-PARS INTERMEDIA; *N*-PARS NERVOSA. FIG. 5*b* REPRESENTS A PARASAGITTAL SECTION OF THE SAME. LETTERS *A*, *I*, AND *N* AS INDICATED ABOVE. *T*-PARS TUBERALIS

anlage and these three lobes that develop from it. The anlage of the pars nervosa is not touched in this experiment, and it undergoes definite growth in spite of the absence of the other lobes of the hypophysis, as shown by Allen ('17) and by Smith ('20). Smith made a careful quantitative study of the later development of this structure, and showed that it is much retarded in growth and abnormal in form as compared with its condition in normal tadpoles of similar size. In cases of partially successful operations, Smith found that any part of the pars nervosa in touch with fragments of the buccal anlage undergoes hypertrophy, thus appearing to respond to the local stimulus exerted by its derivatives. This is made especially clear in cases where the buccal anlage has suffered some displacement. No physiological evidence has been offered to show whether this "vestigial" pars nervosa has any functional value.

Let us now sum up the complex of effects produced by the removal of the buccal anlage and the consequent total absence of the pars anterior, pars intermedia and pars tuberalis.

They are as follows:

1. Failure to metamorphose.
2. Retardation of growth in size.
3. A striking modification of the pigment cells resulting in the assumption of a creamy silver color in *Rana pipiens* and a less conspicuous color change in other forms.
4. An apparent increase in susceptibility to disease and other unfavorable conditions. This needs statistical treatment, but is obvious to those who have worked along these lines.

It will be our object in this paper to discuss only the first two factors, because they involve problems of development (differentiation) and size growth. It has been definitely shown that the pars anterior of the hypophysis is concerned with both these processes, and we have

equally good evidence that neither the pars intermedia nor the pars nervosa is concerned with them. The pars tuberalis is an enigma because of our total lack of knowledge regarding its functions.

Relation of hypophysis and thyroid gland

The interrelations between the thyroid gland and the pars anterior of the hypophysis are quite interesting. Rogers ('18), Larson ('19), Hoskins and Hoskins ('19), and Smith ('20) have all shown that thyroidectomy causes the latter to increase in size, while, on the other hand, Adler ('14), Allen ('16, '17), Smith ('16, '20), and Hoskins and Hoskins ('19) have demonstrated that the removal of the hypophysis causes a retardation in the growth of the thyroid gland and prevents it from storing up colloid secretion. Smith ('20) showed that the thyroid gland of hypophysectomized tadpoles is reduced to one-sixth the normal weight in tadpoles 36 mm. or more in length.

Not only is there practically no visible accumulation of thyroid secretion, but the absence of the hypophysis has the same effect in relation to metamorphosis as does the absence of the thyroid gland. There is no doubt upon this point in the minds of those who have investigated it. Allen ('25) showed that there was the same degree of growth of the hind-legs in tadpoles from which the thyroid gland had been removed, in those that had been hypophysectomized, and in those from which both had been removed. In all three cases of the total absence of both, or the absence of either, the hind limbs develop to the same degree, which is specific to the species in question.

Whatever be the nature of the rôle played by the hypophysis, the secretion formed as a result of its coöperation with the thyroid gland is stored up in the thyroid follicles, not in the hypophysis. Feeding thyroid preparations to tadpoles induces metamorphosis even though the thyroid gland and the hypophysis be absent. We have already called attention to the fact that Allen ('19) caused metamorphosis by feeding iodine to tadpoles from which the hypophysis had been removed and even in those from which both the hypophysis and thyroid glands had been removed.

The hypophysis alone, even when present in unusual degree, is incapable of inducing metamorphosis, or even a tendency in that direction in the absence of the thyroid gland. Allen ('20, '21) demonstrated this point by implanting the hypophysis of adult frogs into thyroidectomized tadpoles. Even in these cases, where the material of the hypophysis was present in excessive amount, there was not the slightest evidence of any progress toward metamorphosis beyond that regularly reached in the thyroidectomized tadpoles, even after a period of many months. The implanted glands maintained themselves during this entire time as shown by a histological study of them made at the conclusion of the experiment.

We stated above that the pars anterior of the hypophysis is the portion of that gland complex that is concerned in cooperating with the thyroid gland to induce metamorphosis. Allen ('21, '27) made implants of the pars anterior, the pars intermedia, and the pars nervosa into hypophysectomized tadpoles; but the pars anterior was alone effective in inducing metamorphosis (fig. 6). We have pointed out that no studies have been made regarding the significance of the pars tuberalis.

It was shown in these experiments that implantations of the pars anterior bring about the secretion of colloid within the thyroid gland, which results in metamorphosis. Histological studies of the

thyroid gland during the progress toward metamorphosis showed a progressive accumulation of colloid substance. While there can be no question about the dependence of the thyroid gland upon the pars anterior of the hypophysis, we are still in the dark as to the nature of this relationship.

Smith and Smith ('23) showed that this same result could be produced by repeated intra-peritoneal injections of extracts of the fresh pars anterior of the beef hypophysis, obtained by grinding the sterile glandular substance in sand, diluting with saline solution and centrifuging. Injection of this preparation three times per week restored the thyroid gland of hypophysectomized tadpoles to completely normal function and resulted in metamorphosis of the tadpoles so treated. It is important to keep in mind the fact that metamorphosis was a result of the restoration of the thyroid gland to normal functional activity. This experiment would appear to demonstrate the presence of a secretion in the pars anterior of the hypophysis that influences the thyroid gland or that may contribute substances essential to the elaboration of its secretion.

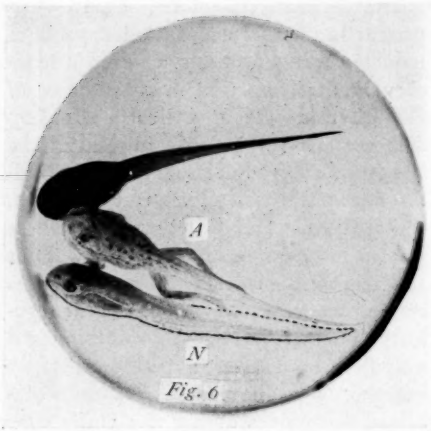

FIG. 6. PHOTOGRAPH OF THREE HYPOPHYSECTOMIZED TADPOLES OF RANA AURORA DRAYTONI INTO EACH OF WHICH A DIFFERENT PORTION OF THE HYPOPHYSIS OF THE ADULT FROG HAS BEEN TRANSPLANTED

These are as follows: into *A*-Pars Anterior; into *I*-Pars Intermedia; into *N*-Pars Nervosa. The reëstablished development of the Pars Anterior transplant and the color change of the Pars Intermedia transplant are obvious.

Spaul ('25, '28) devised a method of making an extract of the pars anterior of the hypophysis by grinding it up in a 0.125 per cent aqueous solution of acetic acid. When injected at frequent intervals—three times per week—this induced metamorphosis of normal tadpoles. Comparisons of the effects of thyroid and pars anterior injections in uniform weak dilutions showed the former to be far more potent than the latter.

Immersion of tadpoles in pars anterior solutions wholly failed to induce metamorphosis, showing that absorption through the skin and probably also through the alimentary tract fails to induce metamorphosis.

Spaul makes an interesting observation upon the behavior of tadpoles injected with pars anterior extract as compared with those injected with thyroid extract. The specimens injected with the latter made quick rapid movements in contrast with the more quiet behavior of those injected with the pars anterior extract.

Effect of metabolic depressants

Huxley ('25) had shown that KCN or alcohol inhibits metamorphosis through a depressant effect upon metabolic processes when used in sufficiently high non-toxic amounts in the medium. In this way it can to a large degree counteract the influence of the thyroid gland. Spaul ('28) applied the same methods of investigation to determine whether the effects of intra-peritoneal injections of the pars anterior of the hypophysis could

be similarly nullified. He found that this was true in correspondence with the findings of Huxley. A similar decrease in the ability of the tissues to respond to the stimulus of the secretions of the thyroid gland or of the pars anterior of the hypophysis was shown in the case of tadpoles that had been subjected to the action of X-rays. These experiments showed the degree to which injury or inhibition of the tissues could lessen their capacity to respond to stimulus.

The nervous system is not involved in the response to these stimuli, as Huxley ('25) showed by narcotizing with urethane. This treatment does not inhibit or retard metamorphosis of tadpoles in response to thyroid extracts in the aquarium medium; thus demonstrating that the hormone does not act through the nerve centers. Spaul ('28) applies the same method of investigation to the treatment with extracts of the pars anterior of the hypophysis and comes to the same results, confirming Huxley's conclusions in this regard.

Unreliability of commercial preparations of endocrine substances

Hoskins and Hoskins ('20) caused normal and thyroidectomized tadpoles to metamorphose by administering to them a commercial preparation of the pars anterior of the beef hypophysis prepared by one of the leading manufacturers of endocrine preparations. They had an analysis made which showed that this preparation contained iodine in the ratio of 1:200,000 in the fresh gland. They did not know the form in which it occurred but assumed that it would be soluble and diffuse into the water of the aquarium in which the tadpoles were kept. They concluded from these experiments that feeding the pars anterior of the hypophysis causes metamorphosis.

Smith and Cheney ('21) repeated this work and likewise produced metamorphosis by feeding tadpoles with the same commercial preparation of anterior pituitary used by Hoskins and Hoskins. They made a crucial test, however, by preparing their own anterior pituitary material from fresh glands and under laboratory conditions. Feeding this material to tadpoles, they did not produce any tendency toward metamorphosis. Analysis showed that the commercial preparation which induced metamorphosis contained 120 times the amount of iodine found in their own laboratory prepared material. Smith and Cheney thus rightly conclude that the pars anterior of the hypophysis does not induce metamorphosis when fed to tadpoles. The whole question is one of contamination of a pharmaceutical product and serves to point a moral regarding the caution that must be observed in the use of commercial preparations in scientific experiments.

This work is completely in accord with unpublished investigations of the writer, who in 1918 induced metamorphosis in *Rana pipiens* by feeding it the same make of anterior pituitary preparation used by Hoskins and Hoskins. When we later repeated the experiment with preparations made in the laboratory from fresh glands, there was no trace of metamorphosis. These experiments were carried out upon hypophysectomized, thyroidectomized and normal tadpoles.

Effect of the hypophysis on metamorphosis in the axolotl

Much interest has been shown recently in the relation of the pars anterior to metamorphosis in the axolotl and the results are rather perplexing. Smith ('22, '23, '26) made intraperitoneal injections of fresh anterior hypophysis extract of cattle into the Colorado axolotl and produced a

retardation of metamorphosis. Here we have an effect quite the reverse of that produced by Smith ('23) when he applied the same method of treatment to Rana tadpoles both normal and hypophysectomized as described above. This experiment was controlled by injections of Ringer's solution posterior lobe extract and by muscle extracts. Some of his animals were injected with the anterior hypophysis extract alone, while others received a mixture of anterior hypophysis and thyroid gland, serving as an important test for comparing the results with those in which thyroid extract alone is injected. Smith carried out this work in the thorough and careful manner that characterizes his work, with the uniform result of retardation of metamorphosis of the Colorado axolotl.

Hogben ('23) made intraperitoneal injections of a commercial preparation of anterior hypophysis into the Mexican axolotl and caused metamorphosis. Spaul ('24) repeated the experiment, using the same commercial preparation employed by Hogben, and likewise induced metamorphosis. Spaul ('24) in a later investigation tested twelve commercial preparations of pars anterior of the hypophysis and produced metamorphosis with only two of them. Hogben ('27) in his admirable little book upon the internal secretions concedes "Experiments with commercial extracts are however, to be regarded as having doubtful value." This pitfall has been avoided in more recent experiments by Spaul ('25), by which he produced metamorphosis in the axolotl by injecting aqueous acetic acid extracts which he himself had prepared, and Hogben states in his book ('27) that he has attained the same results in unpublished researches. Spaul ('25) attributes Smith's failure to induce metamorphosis in the axolotl to the use of a weaker solution and to contamination with the posterior lobe but this latter objection is hardly a valid one because Smith used a posterior lobe extract as a control and failed to cause retardation of metamorphosis.

Uhlenhuth and Schwartzbachen ('28), by the use of extracts prepared by the method of Spaul, accelerated the metamorphosis of larvae of the Utah axolotl by 36 days as compared with the controls. He adopts Spaul's explanation that Smith's failure to induce metamorphosis is due to contamination of the extract with adherent material of the posterior lobe of the hypophysis. Whether this is the true explanation should be determined by more direct experiments with the posterior lobe itself. The reader will have to judge regarding the merits of this controversy, because the writer feels unequal to the task; although it must be said that the preponderance of evidence is at the present time in favor of the view that the intra-peritoneal extracts of the hypophysis do induce metamorphosis in the axolotl. This would certainly be in line with its universally admitted tendency in anuran tadpoles.

Uhlenhuth and Schwartzbacher ('28) show that intraperitoneal injections of pars anterior of the hypophysis are entirely impotent in inducing metamorphosis of *Ambystoma tigrinum* if the thyroid gland is absent. This was true in larvae of the Utah axolotl form of this species.

In summing up our conclusions upon this point, we may say that *implantation* of the living pars anterior of the hypophysis or frequently repeated intraperitoneal injections of emulsions or extracts of this gland fresh or dried, induce metamorphosis in amphibians provided the thyroid gland is functional. Some may wish to follow Smith in making a reservation regarding the potency of this gland

in the case of the axolotl. Even so, that would constitute a special case that would not invalidate the general principle which is now well established. It is now generally conceded that *feeding* anterior hypophysis to amphibian larvae does not induce metamorphosis or any tendency toward it. We can only conjecture as to why this mode of administration is ineffective in accelerating metamorphosis even when the thyroid gland is present. Experimental studies alone can give the answer.

It is furthermore established that the pars anterior of the hypophysis acts upon the process of metamorphosis only through its influence upon the thyroid gland. As to the nature of this influence we again can only conjecture. One point of great significance is the fact that there is no accumulation of thyroid secretion without the influence of the pars anterior of the hypophysis, as is clearly seen in the lack of colloid in the thyroid gland of hypophysectomized tadpoles and its appearance after transplantation of the pars anterior or repeated injection of its extracts. While pars anterior may play an important part as a releasing mechanism for causing the thyroid gland to discharge its secretion into the blood, as urged by Uhlenhuth, the foregoing facts show that it is certainly essential to *production* of the secretion.

Ingram ('28) gives us an insight into the significance of the influence exerted by the pars anterior upon the thyroid gland by showing that heteroplastic transplantation of the pars anterior of the early metamorphosing *Rana clamata* into the slow metamorphosing tadpoles of *Rana catesbiana* accelerates metamorphosis in the latter form. It must be said that he used three gland implants from metamorphosing tadpoles in this experiment and one might be inclined to interpret the accelerated development as a result of the quantity instead of the quality of implanted glandular tissue. Examination of the thyroid glands of the *Rana catesbiana* hosts showed that their thyroid glands had increased to twice the size of those of the controls. The cells of the thyroid glands had increased in length and there was a decrease of colloid secretion. This condition resembles that described by Uhlenhuth as characteristic of the thyroid gland in process of actively discharging its secretion. This experiment suggests the view that the early metamorphosis in *Rana clamata* and the delayed metamorphosis in *Rana catesbiana* might be determined primarily by the activity of the pars anterior of the hypophysis, rather than by differences in the thyroid glands. Much work is necessary to give us the basis of a decision upon this interesting question.

Effect of the hypophysis on growth in size

While it is clear that the pars anterior of the hypophysis affects metamorphosis by enabling the thyroid gland to produce its secretion, it is equally certain that a secretion elaborated by it causes growth in size. Smith ('18, '20) has accurately demonstrated the fact that feeding preparations of the pars anterior induces growth in size and no one has contested this point. The observations of the writer fully bear out his findings in this regard. Smith and Smith ('23) showed that frequent intra-peritoneal injection of pars anterior extracts caused hypophysectomized tadpoles of *Rana boyeli* to increase in three months to a volume three times that of normal uninjected controls, while this treatment caused normal tadpoles to increase in a similar period of time to twice the volume of the uninjected tadpoles. Thyroidectomized tadpoles were even made to exceed their thyroidectom-

ized controls by four times their volume as a result of pars anterior injections.

Not only has growth acceleration been attained by administering anterior hypophysis to tadpoles, but it has likewise been demonstrated by Uhlenhuth ('21, '23) in *Ambystoma*, by experiments in which he fed chopped worms, beef liver, and pars anterior of the hypophysis to different sets of young *Ambystoma tigrinum*. ing sets of three litter-mate young female rats, performing thyroidectomy upon two and then treating one of the latter with daily intraperitoneal injections of pars anterior extracts. The animals thus treated showed normal growth while the thyroidectomized individuals that were not so treated showed all the growth deficiencies of typical cretinism. They concluded that the growth deficiencies of

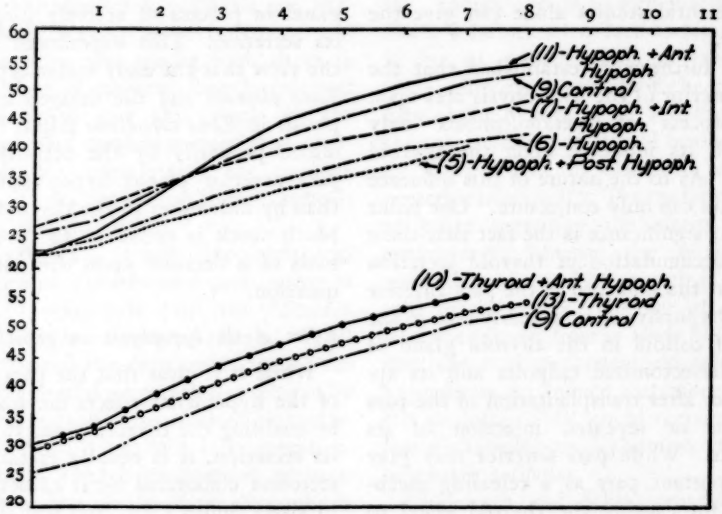

FIG. 7. GRAPHS SHOWING THE RATE OF GROWTH OF TADPOLES OF RANA AURORA DRAYTONI STUDIED IN 1925

The numbers in parentheses indicate the number of specimens averaged in the group indicated. The abbreviations are self-evident. Controls are normal tadpoles and the line indicating their growth is repeated in the upper and lower group. Ordinates indicate total body length in millimeters and abscissae mark the time from the beginning of the experiment measured in weeks.

The liver produced an initial acceleration of growth comparable to that caused by pars anterior feeding, but the latter caused persistence of growth long after it ceased in those fed with worms or liver. There thus appeared to be a specific influence exerted by the pars anterior in prolonging the growth period.

Flower and Evans ('25) demonstrated the influence of the pars anterior of the hypophysis in cases of cretinism by choos- cretinism are due to a disfunction of the hypophysis resulting from the absence of the thyroid gland. This conclusion seems reasonable in the case of the mammals upon which these experiments were performed. In the tadpoles, on the other hand, thyroidectomized individuals keep pace in their growth with normal specimens until the latter begin to undergo metamorphosis. It is difficult to say how large thyroidectomized tadpoles may ul-

timately grow but they reach twice the total length attained by normal tadpoles during normal larval growth. We are here dealing with continued larval growth rather than accelerated growth. Interesting problems are presented in this field.

Allen ('20, '21, '28) showed that transplantation of the pars anterior into hypophysectomized tadpoles causes them quickly to attain the normal growth in total length that had been denied them by the extirpation of the hypophysis. This treatment likewise appeared to cause thyroidectomized tadpoles to increase slightly in length, and a small number of specimens from which both the thyroid and hypophysis had been removed were made to show growth acceleration in response to implantation of the pars anterior, but the number of cases was too small to give positive proof on this point. It is perfectly certain from these experiments that implantation of the pars anterior fully restores growth from subnormal to normal size and that implantation of the pars intermedia or of the pars nervosa has no effect upon growth—neither accelerating nor retarding it. Figures 7 and 8, taken from a recent paper by the writer, illustrate this point. These results are apparently less striking than those of the Smiths ('23), but it must be kept in mind that these are linear determinations as compared with their three dimensional volumes. These experiments should be still further extended to determine the interrelation between the pars anterior and the thyroid gland, but we may safely conclude, especially in view of the striking growths induced by the Smiths in thyroidectomized tadpoles, that the pars anterior of the hypophysis

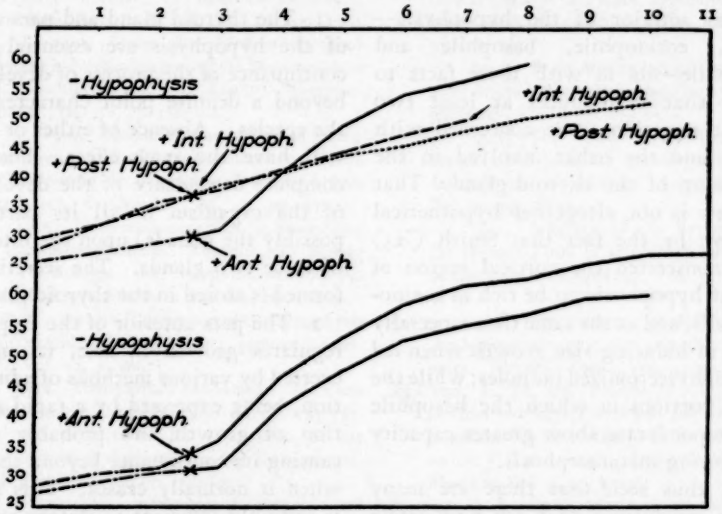

FIG. 8. GRAPHS SHOWING GROWTH OF HYPOPHYSECTOMIZED TADPOLES OF RANA AURORA DRAYTONI

At the time marked by X, implants of different lobes of the hypophysis were made as indicated by the abbreviations. The glandular material implanted was in each case taken from the same adult frog. Ordinates indicate total body length in millimeters and abscissae mark the time from the beginning of the experiment measured in weeks.

can induce size growth in the total absence of the thyroid gland.

This is most significant in view of the fact that it cannot induce *metamorphosis* without the coöperation of the thyroid gland, which indeed seems to play the chief rôle in that regard. There is much significance too in the fact that feeding the pars anterior induces size growth but does not induce metamorphosis. The fact that there are three types of cells in the pars anterior of the hypophysis—namely, eosinophile, basophile and neutrophile—fits in with these facts to suggest that it produces at least two different secretions, one concerned with growth and the other involved in the functioning of the thyroid gland. That this view is not altogether hypothetical is shown by the fact that Smith ('23) has demonstrated the cortical region of the beef hypophysis to be rich in eosinophile cells, and at the same time especially potent in inducing size growth when fed to hypophysectomized tadpoles; while the central portions in which the basophile cells preponderate show greater capacity for inducing metamorphosis.

It is thus seen that there are many definite conclusions that can now safely be drawn regarding the functions of the thyroid gland and pars anterior of the hypophysis in connection with their control of growth and development. It is hoped that this survey may do more than outline our present knowledge of this complicated field; it will prove far more worth while if it should induce any of the readers to attack some of the many problems that are as yet unsolved. We wish to point out the advantage of using amphibian material. The removal of these glands at their inception, the ease of transplantation technique, the use of injections and of hormone containing media all have served to give us a wonderfully clear picture of the rôles played by these glands, and the field is a large one. Investigations along these lines have just begun.

SUMMARY

1. The thyroid gland and pars anterior of the hypophysis are essential to the continuance of the process of development beyond a definite point characteristic of the species. Absence of either or of both will have the same effect. There is a complete dependence of the development of the organism in all its parts (save possibly the gonads) upon the interaction of these two glands. The secretion thus formed is stored in the thyroid gland.

2. The pars anterior of the hypophysis regulates growth in size, its influence, exerted by various methods of administration, being expressed by a rapid acceleration of growth and probably also by causing its continuance beyond the period when it normally ceases. This stimulus is certainly sufficient to restore growth to normal when administered to individuals in which the pars anterior secretion has been sub-normal or absent, and it appears possible to stimulate growth to a fair degree beyond normal by administration of the pars anterior secretion in various appropriate ways.

3. This function of the pars anterior of the hypophysis whereby it induces growth in size appears to be quite independent of the thyroid gland.

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THYROID AND GROWTH

By FREDERICK S. HAMMETT

The Research Institute of The Lankenau Hospital, Philadelphia

THE anatomist sees in the thyroid a bi-lobar structure embracing the trachea (61), the histologist a collection of vesicles containing a pink-staining homogeneous mass surrounded by cuboidal cells (5). The physiologist sees a gland of internal secretion (48), while to the chemist the thyroid is the beaker in which a benzene ring is iodized (36). To the owner of an overly active organ it is an unmitigated nuisance.

These concepts as entities have occupied the time of hundreds of workers who have deluged the scientific and pseudoscientific journals with thousands of articles. It is neither possible nor necessary that a reference list of all this work be made a part of the discussion. The reader who wishes to wander through the capillary bed of the literature will find the chief points of departure indicated in the references which are given, and in the compilations of Biedl (3), Swale Vincent (81), and Sharpey-Schafer (73).

The statement that the chief function of the thyroid is a regulation of the metabolic rate (38), while true, epitomises the point of view of the laboratory worker, in that it envisages no relation of this fact to the broader biological aspects of the phenomenon. The biologist, given the limited conclusion, wishes to know what factors are of influence in changing the functional capacity of the organ, what the results of these changes are in the individual, and what they imply as to the part played by the structure in organic and human development, or growth in its widest sense.

The phenomenon of growth is ubiquitous and of importance to man. From the growth and productivity of vegetable life (44), to the growth of man as an individual (69), and in the mass as populations (58), not to omit the aberrations such as cancer which destroy life (16), the question of growth is inextricably tied up with all matters of human interest. It is from such a point of view that this presentation of the relation between thyroid and growth is made.

The environmental factors known to influence the level of thyroid activity will be first considered. It is convenient to group them into endogenous and exogenous. It is not to be understood that this division implies a lack of inter-relationship, for quite the contrary is the fact. This is no place, however, to indulge in analytical gymnastics over the matter.

ENDOGENOUS FACTORS IN THYROID ACTIVITY

The classical example of an endogenous factor is the congenital absence or functional diminution to ineffectualness of the thyroid gland. The result is an athyreotic individual in the first case and a cretin or human dwarf of a well recognized type in the second (59).

The early ablation of the thyroid from sheep (75) or other experimental animals sometimes, but not always, results in a markedly stunted individual (21). Such specimens should not be called cretins,

for the latter, as stated above, result from a congenital developmental defect (65), which produces quite a different picture from that following thyroid removal. The histological studies of Kull (45), Rumph and Smith (71), and others (2) indicate that the fetal thyroid may indeed be functionally active some time before birth in the normal individual. If such be true it is obvious that the congenital absence of the organ would have quite different effects on development than would experimental ablation even in the new-born.

Some observations suggest that hereditary and familial factors may be inductive of disturbances in the level of thyroid activity (42; 46; 17). As far as I know, however, the data have yet to be critically analysed.

SEX AND THE THYROID

Another possibly congenital, but nevertheless real endogeneous factor is sex.

An enlarged thyroid, commonly called a goiter, is a sign of quantitative if not qualitative alteration in glandular activity (4). Old records state and paintings of early artists such as Botticelli attest the fact that a slight swelling of the throat, which we now know to be due to thyroid enlargement, was considered an attribute of beauty. Even a cursory inspection of the early paintings impresses one that this peculiarity was almost exclusively found in women. In modern times recognition of the sex difference in incidence is evidenced in the advertisements for cures of the disorder found in the *Police Gazette* and other like advertisers of spurious proprietary remedies. Here too the caricatured sufferer depicted is always a woman.

This popular impression is borne out by the statistical studies of Marine and Kendall (53), Levin (47) and others. These show that to-day, as always, the incidence of thyroid disturbance is greater in girls and women than in boys and men.

The basis of the difference undoubtedly lies in the difference in the sex physiology and the sex difference in relation of the gonadal incretory activities to thyroid activity (13). It is a well known fact that thyroid enlargement frequently occurs in women during the shifts in ovarian activity associated with menstruation, pregnancy, and the menopause (65). These can justly be considered causal factors of thyroid disturbance, and, being absent in the male, as contributors to the sex difference in goiter incidence. Consistent with this is the fact shown in an analysis of the weight correlations of thyroid and gonads of sexually mature albino rats, that positive association, as mediated by the adrenals, seems to be stronger in the female than in the male (22). Finally, marked sex differences in degree of growth retardation following thyroid removal are found, as will be shown presently.

Thyroid enlargement at puberty is a common occurrence. The peak of the incidence curve of simple physiological goiter is associated in both sexes with this coming into activity of the incretory function of the reproductive system (47). As will be shown later, puberty also conditions a marked change in the reaction to experimental thyroid deficiency.

All these give ample proof that sex factors are endogenous determinants of the level of thyroid activity.

Emotional excitability is also an endogenous factor of influence. Clinical records contain many reports of thyroid enlargement directly traceable to emotional stress (60; 56). This was particularly noticeable during and immediately after the World War (14).

THE INFLUENCE OF DIET

Foremost among the immediate exogenous factors is dietary deficiency. The responsible substance in most cases is iodine (15).

In the consideration of the influence of diet it is necessary to differentiate between the character and the iodine content. McCarrison (49) has recently reported thyroid disturbance dietary in origin and seemingly unrelated to iodine. A vitamin deficiency such as causes scurvy also may affect thyroid function (55). I myself have increased the weight of the thyroids of albino rats from one to two hundred per cent above the usual by giving the animals nothing but meat, and have cut the size to half or less by giving them nothing but lettuce. Thus the character of the diet is of importance (74), although it may be that the reactions will ultimately be traced back to inadequate iodine, that is to say, an iodine ingestion inadequate for the strain put upon the thyroid by the unsuitable diet.

Now a diet deficient in iodine is so because its food-stuffs are iodine poor. The mineral composition of food-stuffs is directly related to the available nutrients in the soil on which they are grown. Therefore the iodine content of the diet is related to the geographical or geological distribution of iodine in the soil and potable waters from which it is derived. Thus geographic location and geologic formation are important factors in determining the level of thyroid activity. These facts have been largely worked out by the painstaking efforts of McClendon (52) and his co-workers. To illustrate the point Figures 1 and 2 from his publications are given. The first represents for the United States the regions of low and high iodine content in soil, water, and food. The second shows the incidence of simple goiter in the same regions. The negative correlation is striking. Such geographic differences are not confined to the United States. Kendall (40) has found that thyroids of abattoir animals in this country tend to be much poorer in the essential element than those of England. These world-wide differences indicate the importance of geographic or geologic factors.

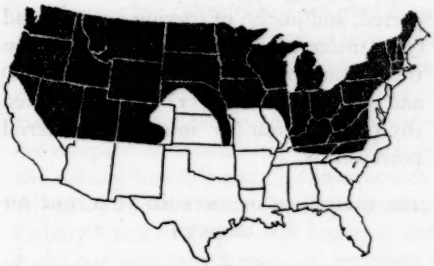

FIG. 1. THE IODINE IN DRINKING WATER IN THE UNITED STATES

In the black area, waters contain from 1 to 22 parts of iodine per hundred billion parts of water; in the white area, from 23 to 18,470 parts. Courtesy Jour. A. M. A. (From McClendon and Hathaway.)

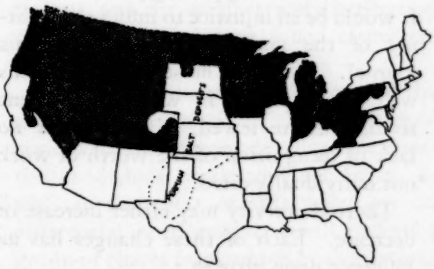

FIG. 2. SIMPLE GOITER IN THE UNITED STATES, FROM DATA OF THE DRAFT BOARD

In the white area there were from 0 to 5 military goiters per thousand drafted men; in the black area, from 5 to 111. Courtesy Jour. A. M. A. (From McClendon and Hathaway.)

Allied to the geographic factor is that of climate or season. Seidell and Fenger (72), and Kendall and Simonsen (39) report a definite seasonal variation in iodine content of the thyroids of slaughterhouse animals. Riddle and Fisher (68)

found seasonal changes in thyroid size in pigeons. No matter whether these changes are direct reactions or mediated by other endogenous or exogenous influences, the fact remains that season is a factor conditioning the level of thyroid activity.

Finally it has been found that infections and parasitic infestations (1) are frequent exogenous initiators of thyroid disturbance. Though focal infections are suspected, and justly, of stirring up the gland (64), interest has been largely centered on the demonstration by McCarrison (50) and his co-workers (51) of the marked thyroid reaction to intestinal bacterial putrefaction.

THE INFLUENCE OF THYROID FUNCTION ON GROWTH

The environmental factors known to produce changes in the level of thyroid function have thus been briefly sketched. The influences of these changes on growth and development will now be discussed. The literature is appallingly voluminous. It would be an injustice to inflict the printing of the mass of references on this journal. Therefore most of my citations will be to papers in which antecedent studies are reviewed. This implies no lack of recognition of the worth of work not individually cited.

Thyroid activity may either increase or decrease. Each of these changes has an influence upon growth.

When thyroid function is deficient, either by accident as in cretinism, or by design as in experimental ablation, growth is retarded (23). When such stunted individuals are given thyroid, growth is accelerated (66; 76). From these facts as well as from a priori considerations it is assumed that the administration of thyroid by feeding or other means to normal subjects is a valid method of producing in the organism a condition analogous to an increase in thyroid functional level. Such an increase in the initially normal animal may result in either acceleration or retardation of growth (7; 24). The size of the dose administered determines which way the cat will jump. If the amount given does not increase total metabolism to the point where catabolism predominates, growth in weight is hastened. If the amount is large enough to put anabolism in abeyance, so that more energy is expended than can be assimilated, growth is slowed. This reaction occurs whether whole gland substance is used or the crystalline iodine-containing hormone thyroxin (8) first isolated by Kendall (41). Differential organ hypertrophy results from such acceleration in rats and rabbits, though recovery tends to follow the discontinuance of high thyroid feeding (9). These short time experiments serve to show that distortion of bodily proportions is producible by increase in thyroid function.

Alteration of differential development resulting from excessive thyroid activity is not confined to mammals. The studies of Romeis (70), Gudernatsch (20), Swingle (78), Uhlenhuth (80), Drzewicki (11), and others, have well demonstrated the intrinsic importance of thyroid functional level on structural development and allied phenomena in Amphibia, Reptilia and like forms. Metamorphosis can be accelerated, retarded, or inhibited at will according to the experimental procedure used.

In the fowl also, as representative of the family Aves, it has been found that hyperthyroidization produces definite structural alterations (57; 37; 82; 18; 43). Even the Insecta have not escaped the attention of the all-curious scientist in this field (67). But here the data are complicated by the

fact that structures analogous to the thyroid have yet to be surely identified in this group of organisms.

In the family Pisces much work has been done with trout by Marine (54). Here, however, the interest has been chiefly in the elucidation of the cause and prevention of the goiter to which the species is susceptible, and but little if any in functional or structural modifications. It should be marked in passing that diet and iodine separately have been found to be factors influencing thyroid size in fish as in other forms.

All these observations attest the ubiquity of developmental disturbance induced by increased thyroid activity.

Lowered thyroid activity, or thyroid deficiency, also has a definite influence on growth. But here gross growth is always retarded. This is because the assimilative processes can only change in one direction when a metabolic stimulus is lessened or withheld. They must decrease. The pace slackens and the growth increment per unit time decreases.

The fact of this growth retardation has been established by countless experiments on many different species of animals. It is an old story in which the characters are many. The parts they have played in the development of the tale is told in my series of studies of the rôle of the thyroid in growth and need not be repeated here.

CHANGES IN DIFFERENTIAL DEVELOPMENT

Of more recent interest is the search for the answer to the question as to whether the growth retardation is accompanied by a distortion of differential development. The answer will be given as written by the thyroidless albino rat (*Mus norvegicus albinus*).

The data to be considered are the growths of the body and organs of the tests in terms of that of their litter mate controls. Male and female animals of six different ages were used, viz. 23, 30, 50, 65, 75 and 100 days at time of thyroid removal. This was done so that a picture of the rôle of the thyroid in growth at different stages of development would be obtained. All were allowed to grow until 150 days of age, when the animals were killed, the organs removed and weighed and the records completed. Basic figures were given by other organ weights from other rats dissected at the ages of initiation of thyroid deficiency. Thus there was made available material for calculation of the growth increment. Males and females were separated at weaning so as to avoid the mating variable and its consequences. All the rats were from the Experimental Colony Stock of The Wistar Institute and had a common inheritance. Controls and tests were kept under identical conditions of diet and environment. Only those tests were used in the final analysis in which no trace of thyroid tissue was found at autopsy. Further details of the technic and the number and distribution of the animals will be found elsewhere (23; 26).

As I wish to discuss the influence of the age of the animal at the time of thyroid removal on subsequent development under the conditions of thyroid deficiency, as well as the effect of this deficiency on differential development, I will present a group of charts from which both relations may be easily visualized. With some modifications these are the same as those published in my final paper in the *American Journal of Physiology* (27). In these figures age is charted on the abscissa, and the percentage increment of the test structure in terms of that of the control on the ordinate. Thus the height of the line above the base at any given age point tells how much less or how much more the structure grew in the thyroidless animal

than in the control during the interval between thyroid removal and 150 days of age. The influence of increasing age at time of initiation of the glandular deficiency on subsequent development is ascertained by following the lines from left to right. These are not weight but increment values. A process as well as a condition is being visualized.

Now it would be possible to take any one of the several structures studied as a basis of reference for the inquiry as to whether or not differential development is distorted in conditions of thyroid deficiency. While such a procedure would give the answer, it would make difficult a determination of the reaction of the organism as a particulate entity. As this is a desideratum, body weight has been chosen as the reference base. This is represented in the charts by the heavy continuous line. The growth increments of the other structures as percentages of the normal are given by the lighter or discontinuous lines. As with one exception growth of all the organs was retarded by thyroid deficiency, a line above the body weight base means that the particular organ represented was less retarded than the body as a whole, while a line below indicates the retardation was greater. In many cases growth was not only retarded, it was even rendered retrogressive and weight was actually lost. When this occurs the values become negative and the line dips below the zero ordinate. With this introductory explanation we can now go on to an examination of the data.

An inspection of the charts brings out the fact that the older the animal at time of initiation of thyroid deficiency the greater the subsequent growth retardation. This is not due to the shorter interval for recovery, but is an actual age difference in sensitivity. The conclusion is developed from curves published in another place (26), where it is seen that the initial reaction is less the younger the animal, and that the deviation of the course of growth of the tests from their controls increases with the age of the animal at time of thyroid removal.

This increasing susceptibility to growth retardation with age is attributable to the increasing dominance of growth in cell mass over growth in cell number, and the dependency of the former phase on the anabolic processes, which have been shown to be markedly subject to the level of thyroid activity (63). It is evidence for the conclusion that the thyroid is more concerned in growth by increase in cell size than in growth by increase in cell number.

THE THYROID AS A REGULATOR OF THE METABOLIC RATE

Considerable effort has been expended in the attempt to determine the rôle of the thyroid in cell division. Critical examination of the work of those who claim a specific stimulative influence uncovers a lack of appreciation of the fact that thyroid substance itself contains nutrient material aside from the hormone thyroxine (12; 40; 77). Such uncontrolled results hardly merit conclusion. Careful workers, using adequate control as to dosage and material, have not found much. Carrel in a personal communication writes that "We tried thyroxin on pure cultures of fibroblasts some years ago, only from the point of view of a possible effect it might have on the rate of growth. We have never observed any acceleration. Our results have not been published." Butler (6) came to a like result with eggs of *Arbacia*. Gray and Loeb (19) state that—"administration of thyroid gland substance is not followed by a phase of stimulation, but . . . . within the first

two weeks a period of depression sets in . . . ." These authors worked with guinea-pigs and the thyroid was the organ studied. Torrey, Riddle and Brodie (79) showed that thyroxin accelerates certain metabolic processes in *Paramecium*, but does not stimulate cell division. These observations, combined with the well-established facts as to the general metabolic function of the thyroid, justify the conclusion that the rôle of the gland in growth is that of a participant in the regulation of the metabolic rate, through which is determined the level of the maintenance processes of the organism and hence the amount of material presented to the cells for growth purposes during a given period, and that it offers no specific stimulus to growth by increase in cell number.

Thus it is seen that during the period of most rapid growth and up to the time when the curve becomes asymptotic, age is a potent factor in determining the degree of reaction to disturbances of thyroid function.

The charts also show that sex is a factor, for in general, the growth retardation is greater in the female than in the male. The direction of difference is the same as that in normal rats. That is to say, just as the degree of thyroid determined retardation is greater the less the rate of normal growth on age, so is the degree of retardation greater in the female, whose growth is normally less than that of the male. The fact that the sex difference in reaction to thyroid deficiency is correlatable with the sex difference in normal growth shows the interpretation of the age difference in reaction to be well taken.

While the sex (male-female) difference is attributable to sex-inherent differences in general growth capacity, the coming into activity of the sex organs at puberty is another matter. In the one case we are dealing with congenitally determined differences in chromosome constitution with their influence on general growth; in the other we are dealing with the physiological changes due to the influence of gonadal incretory activity. A study of the charts brings out the fact that puberty, which begins in the rat at about 65 days of age, determines a definite shift in the degree of reaction to thyroid deficiency initiated at this time and thereafter.

It is well known that in normal individuals puberty is accompanied by change in growth rate and heightened sensitivity to external influences. It is to be expected that this would be reflected in the reaction to thyroid deficiency. In these investigations the effect is particularly marked in the visceral organs and the thymus (Figs. 5, 6, 7, and 8). Here there is not only a complete inhibition of growth but an actual retrogression or loss of weight. There is no doubt that this is real. It occurs in both sexes.

These pubertal changes are not confined to organ growth. They occur also even in the chemical make-up of the bones (29; 30), blood, and central nervous system of thyroidless animals (31). It is not necessary to make a detailed analysis of the phenomenon. This has been done in earlier papers. All that I wish to point out here is that puberty is an important factor in the determination of the degree of response of the organism to thyroid deficiency.

The analysis of the influence of thyroid deficiency falls into a major and a minor bracket. Of major interest is the answer to the question as to whether differential development is distorted. Of minor interest is the query as to whether the observed differences indicate specific thyroid relationship.

INFLUENCE OF THE THYROID ON THE GROWTH OF DIFFERENT ORGANS

A study of the charts reveals that the organs can be roughly grouped into three classes with regard to their growth retardation relative to that of the body as a whole.

There is the Resistant Group: the eyeballs, brain, spinal cord, body and tail growth in length (Fig. 3), and the long bones (humerus and femur) in both weight and length growth (Fig. 4). The growth of these is in general definitely less retarded than that of the body.

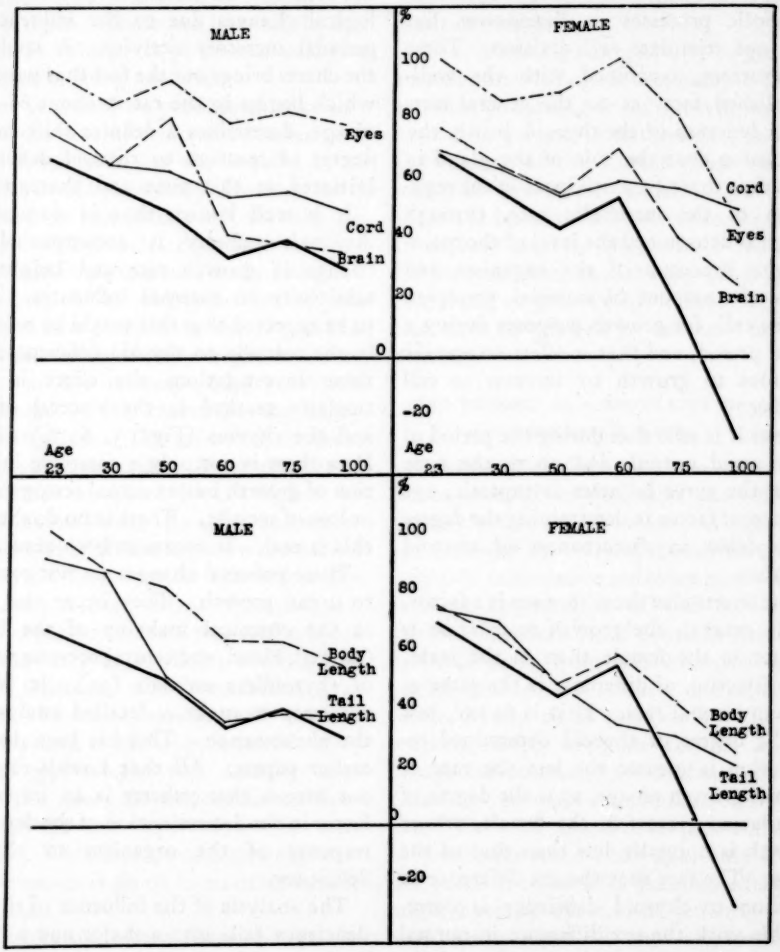

FIG. 3. THE RELATIVE GROWTH RETARDATION OF THE EYEBALLS, BRAIN, SPINAL CORD, BODY LENGTH, AND TAIL LENGTH IN MALE AND FEMALE THYROIDLESS RATS

Reproduction of Figs. 3–9 is made possible through the courtesy of Williams and Wilkins Co., Baltimore

There is the Sensitive Group: the lungs, heart, submaxillary glands, liver (Fig. 5), kidneys, spleen (Fig. 6), adrenals,

Finally there is the Special Group: the testes, epididymis, thymus (Fig. 8), and the hypophysis (Fig. 9).

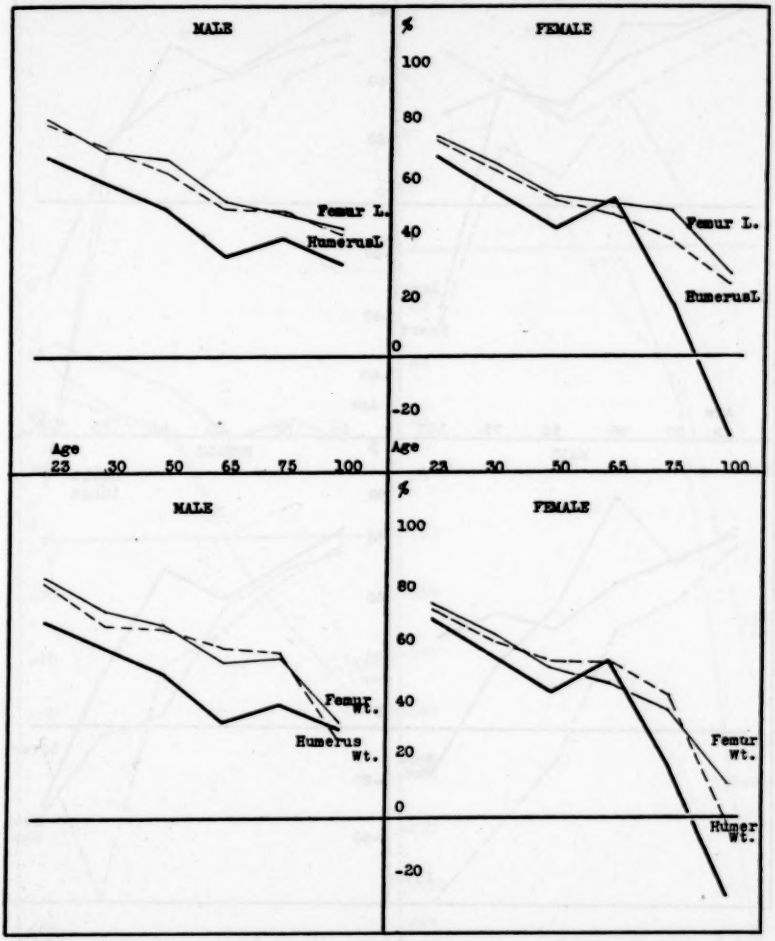

FIG. 4. THE RELATIVE GROWTH RETARDATION OF THE LONG BONES IN MALE AND FEMALE THYROIDLESS RATS

pancreas (Fig. 7) and the ovaries and uterus after puberty (Fig. 8). The growth of these is markedly more retarded than that of the body as a whole, indeed in many cases it is rendered retrogressive.

The testes and epididymis are set off because their growth is largely determined by their specific function of production and storage of new cells (32). Their high resistance to the growth inhibiting

influence of thyroid deficiency is strong support for the idea that thyroid activity is more concerned in growth by increase in cell mass than in growth by increase in cell number.

The thymus is put in the special group because of its exquisite sensitivity expressed as devolution to any nutritional or toxic disturbance (33), and because its function is unknown.

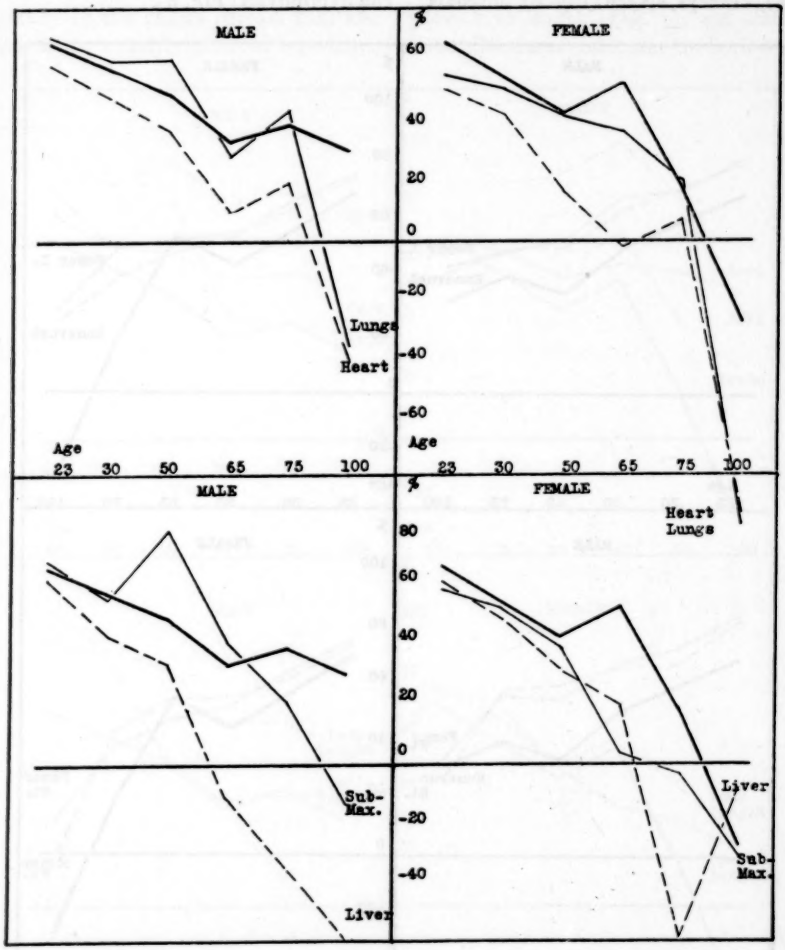

FIG. 5. THE RELATIVE GROWTH RETARDATION OF THE LUNGS, HEART, LIVER, AND SUBMAXILLARY GLANDS IN THYROIDLESS MALE AND FEMALE RATS

The hypophysis naturally falls in the special group because of its well known specific relation to the thyroid (73), which is exhibited in a growth acceleration instead of retardation in conditions of thyroid deficiency.

From these results it is clear that thyroid deficiency produces a distortion of differential development. Because of the the end result is an animal of quite different structural proportions in so far as weight relations are concerned.

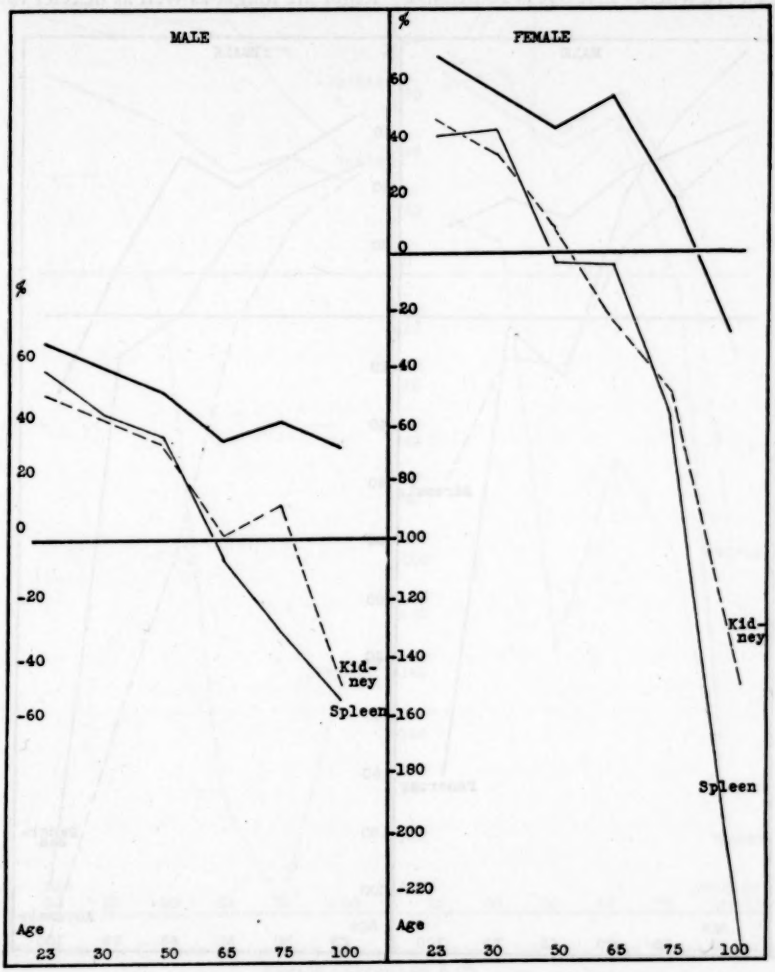

FIG. 6. THE RELATIVE GROWTH RETARDATION OF THE KIDNEYS AND SPLEEN IN THYROIDLESS MALE AND FEMALE RATS

difference in degree of retardation exhibited by the various structures, the proportion of the total which they hold as individuals in the normal is changed and

A further examination of the charts shows that there is a general consistency in the direction of deviation of organ growth development from that of the

body as a whole. This holds regardless of the age at time of glandular removal or sex, save for the exceptions which are discussed elsewhere (27). It is additional evidence for the point that a new structural type of individual tends to be produced. The experimental procedures have yielded an animal in which the nervous and skeletal systems are larger and the viscera of smaller proportions than usual of the total body mass.

Other data show that the humerus and femur are longer as well as heavier than is usual in animals of the body weight recorded, and tend to be ever so slightly longer for the body length (35). This combined with the fact that the body length is less retarded than body weight,

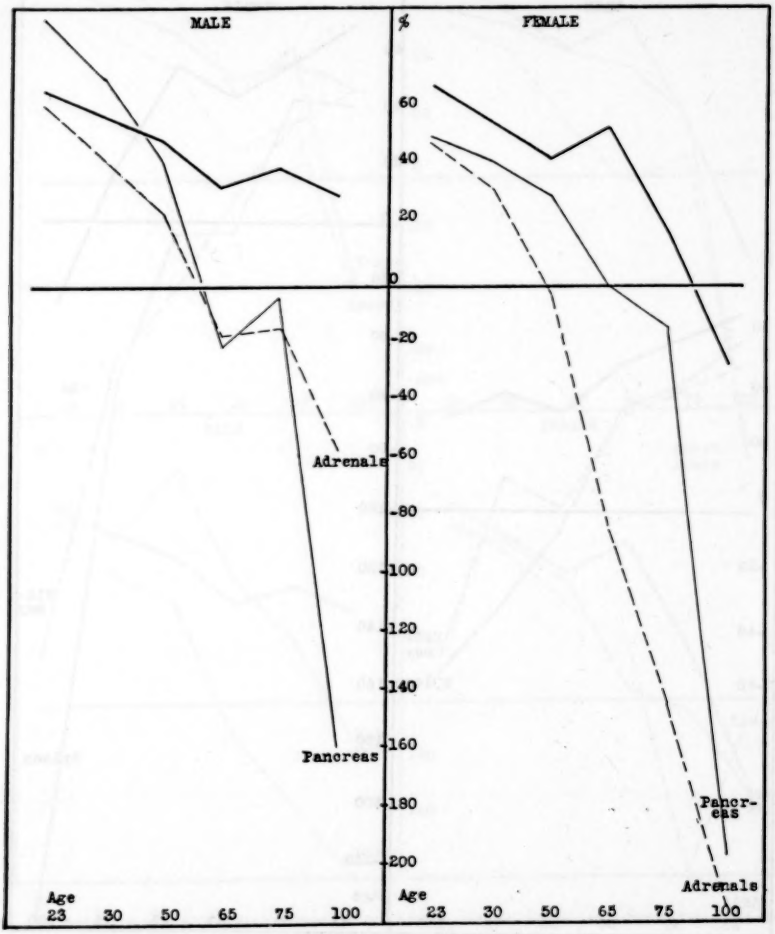

FIG. 7. THE RELATIVE GROWTH RETARDATION OF THE PANCREAS AND ADRENALS IN MALE AND FEMALE THYROIDLESS RATS

indicates that a more slender animal has been produced.

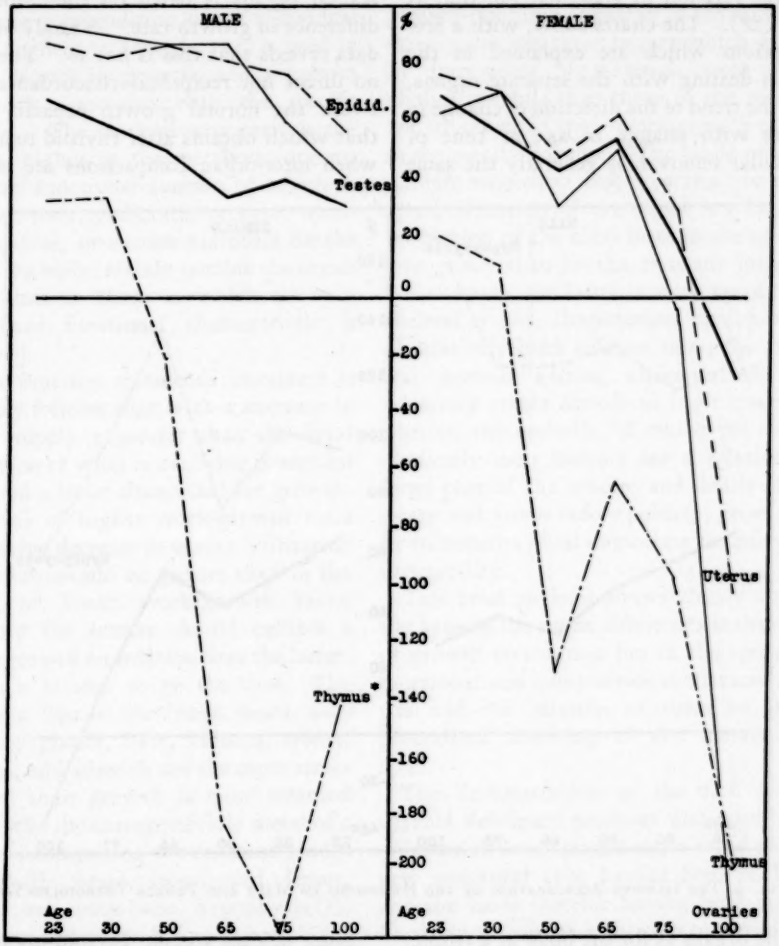

FIG. 8. THE RELATIVE GROWTH RETARDATION OF THE REPRODUCTIVE SYSTEM AND THE THYMUS IN MALE AND FEMALE THYROIDLESS RATS

DIFFERENCES OF REACTION OF ORGANS DUE TO ALTERED METABOLIC LEVEL

Now what is the basis of the organ difference in degree of reaction? Is it an expression of a specific influence of glandular activity on the growth of the individual organ, or is it an expression of the difference in relation to the lowered metabolic level of the fundamental characteristics peculiar to the organ?

In the analysis of the rôle of the thyroid in growth the thesis was developed that the growth retardation of the body as a whole which obtains in conditions of

thyroid deficiency is the result of an essential undernutrition and not of any specific growth relation to glandular function as such (28). The charts show, with a few exceptions which are explained in the papers dealing with the separate organs, that the trend of the direction of change in degree with change in age at time of glandular removal, is generally the same for the organs as for the body as a whole. It is therefore obvious that the major factor is the dependence of the organs on the growth processes of the body as a whole. The conclusion then is that the reaction is due to specific organ constitution and the relation of this to the metabolic level, rather than to any specific influence of glandular activity on the growth of the individual structure.

It might be thought that the difference in degree of retardation exhibited by the several organs is based on their normal difference in growth rate. A study of the data reveals that this is not so. There is no direct nor reciprocal concordance between the normal growth capacity and that which obtains after thyroid removal when inter-organ comparisons are made.

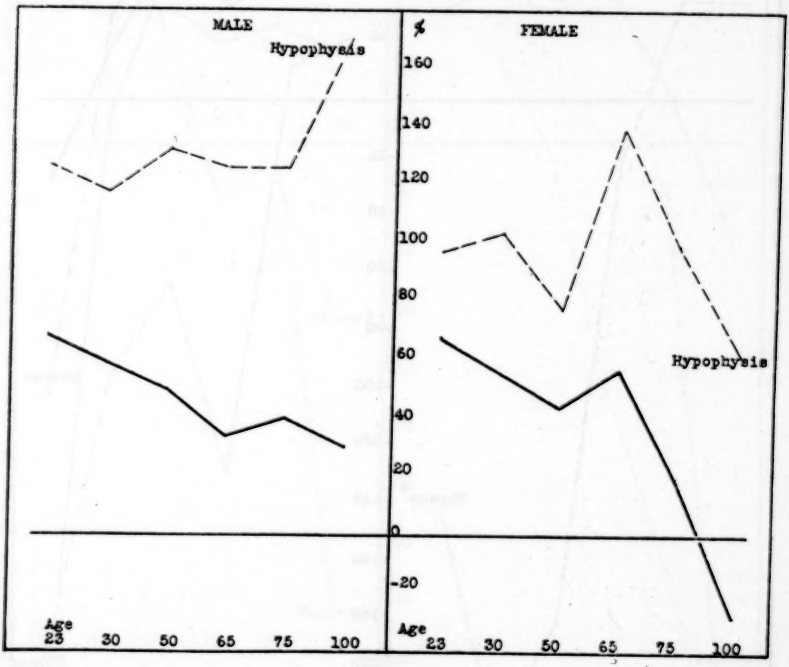

FIG. 9. THE GROWTH ACCELERATION OF THE HYPOPHYSIS IN MALE AND FEMALE THYROIDLESS RATS

Since neither specific thyroid-organ relations nor inherent growth capacity differences are at the bottom of the organ differences in degree of retardation, it is necessary to look elsewhere for the solution.

THE WORK-GROWTH RATIO

Now although growth is retarded, inhibited and even rendered retrogressive,

function continues, else the animals would not continue to live. From this it is clear that function transcends increment. In the energy expenditure of an individual organ incident to living a part is used in repair, a part in growth, and a part in the work associated with the specific function. The work-growth ratio is obviously higher in the metabolic organs, the chief functional concern of which is to work over, elaborate, prepare, transport, secrete, or excrete materials for the rest of the body, mainly outside the organ itself, than in those in which no such generalized functional characteristic is exhibited.

Since function transcends increment it naturally follows that with a decrease in energy supply a greater than the usual proportion of what is available is used for work and a lesser than usual for growth. In organs of higher work-growth ratio the relative decrease in energy utilization for growth would be greater than in the organs of lower work-growth ratio. Therefore the former should exhibit a greater growth retardation than the latter. And such is seen to be the case. The metabolic organs: the lungs, heart, submaxillary glands, liver, kidneys, spleen, pancreas, and adrenals are the more sensitive and their growth is more retarded than that of the non-specifically metabolic structures comprising the resistant group: the eyeballs, brain, spinal cord, femur, humerus, tail, back-bone, hypophysis (?), and uterus and ovary before puberty.

THE METABOLIC LABILITY OF THE ORGAN SUBSTANCES

Associated with the functional characteristics is the nature of the characterizing materials incorporated into the organs during growth. The relative metabolic lability of these is of importance. For the more metabolically labile they are the more readily are they utilized in conditions of inadequate nutrition. The organs which tend to lose weight under the growth-retarding influence of thyroid deficiency are just those organs which grow by increments of materials more metabolically labile than those of the resistant structures of lesser work-growth ratio in the metabolic sense. The labile protoplasmic mass concerned in carrying on the specific function of the organ is a larger proportion of the total mass in the sensitive group than in the resistant group. For example, the latter is made up of the skeletal system, characterized by deposits of relatively inert calcium salts; the central nervous system, characterized by relatively stable lipoids in high concentration; the eyeballs, of which the metabolically inert humors are a relatively large part of the whole; and finally the ovary and uterus before puberty, growing by increments of no immediate functional utilizability.

This brief analysis shows clearly that the basis of the organ differences in degree of growth retardation lies in the specific functional and compositional characteristics and the relation of these to the generalized lowering of the metabolic level.

The demonstration of the fact that thyroid deficiency produces distortion of differential development and a trend to a new structural type having been made, and the bases therefor having been outlined, we are now in a position to consider the implications in the light of what is known of the effect of exogenous and endogenous factors on the level of thyroid activity. Such a procedure is acknowledged to be purely and simply a synthesizing speculation. Apologetics are not required. It is a necessary as well as a legitimate part of scientific endeavor to review the prospect presented from the

eminence of experimental accomplishment and to sketch the terrain spread to view. The contours are there. Whether they have been viewed myopically, hypermetropically, or with astigmatic distortion is a matter for the future to settle.

THE THYROID AS AN ADJUSTOR OF STRUCTURE TO ENVIRONMENT

As a preliminary it is well to fix in mind the fact of the extreme proclivity of the thyroid to size variation. Common observation suggests and statistical analysis establishes the phenomenon as peculiar. I found that in the mature albino rat the thyroid is the most variable of all the structures studied (22). The degree of superiority is so great that it sets the organ apart as unique. If we assume, as I think we have a right to do, that the size variableness of the thyroid is an expression of a corresponding functional variability, we have in this gland a particular mechanism of exquisite sensitivity through which environmental factors may play a significant rôle in the determination of bodily structure.

The geological record shows that profound climatic and seasonal changes have swept over large areas of the earth's surface during past ages (62). Glacial advance and retreat produced ebbings, flowings, and migrations of flora and fauna. Submergence brought the hinterland to the borders of the sea, while emergence threw up new habitable terrains. Thus have occurred shifts in the relative availability of iodine, the element essential for thyroid activity, and for which the sea is the chief source. As Lyell has postulated, these changes were not catastrophic but gradual in their development and recession. They were spread over hundreds of thousands if not millions of years, during which reproductive activity produced thousands of generations of living things.

The consequent shifts in climate and nature of the habitable areas, which were consistent in one direction for long periods of time, were indubitably factors productive of changes in kind and amount of flora. The faunal migrations and scatterings which were similarly induced brought changes in dietary habits and materials.

From the observational and experimental evidence cited at the beginning of this paper it would seem as if these long time uni-directional shifts in environmental factors must indeed have induced changes in the general level of functional activity of the sensitive thyroid. While the type of change in the organ would be dependent on the type of environmental and dietary alteration, it would nevertheless be consistently in one direction according to the direction of shift in environment, and continuous through countless generations.

On the basis of my experimental data it is not beyond the bounds of reasonableness to conclude that conditions such as described would be reflected in the body as a whole, and would be productive of modifications of inter-structural relations in a particular direction. This is all the more probable when it is remembered that the influence of thyroid deficiency on structural alteration is greatly enhanced by the onset of reproductive function; that the degree of alteration is much greater in the female; and that the reproductive system as well as the reproductive capacity of the female is particularly affected (25). Because of this the offspring in successive generations could hardly be expected to escape reflecting the changing trend of the formative parent.

The logical deduction is that thyroid function may well have been a significant participating factor in the production of

varieties within a species if not of species within a genus during the age-long course of evolution of those animal types which possess the gland.

A POSSIBLE MECHANISM FOR THE INHERITANCE OF ACQUIRED CHARACTERS

A further implication is presented.

It is clear that a modification of the relative functional intensity of the several organs is a natural accompaniment of the modification of their weight inter-relationships. This shift can be considered uni-directional since the cause is consistently of the same nature in all groups. Therefore an animal is obtained in which the participation of any single organ in the *totale* of the metabolic processes is different from that normally found. The whole character of metabolism is altered as well as the rate, and altered in one direction.

Now the chromosomes, which are alleged to be the carriers of heritable characteristics, are objects of substance, not ephemeral things, and as such are made up of complexes of chemically simple organic compounds. Bio-physical as well as morphological studies indicate that these compounds are not inert and unreactive, but labile in high degree. It would be strange indeed if the chemical molecules constituting the chromosomes were not subject to chemical alteration by adequate change in the chemical, e.g., metabolic, environment. Such a staticism would hardly be consonant with life. I can see no chemical justification for exempting the germ-cell chromosomes from this principle.

From this premise it follows that adequate chemical agencies could well produce a shift in the nature of the chromosome radicle reaction from which an alteration of offspring character would ensue. It is conceivable that a potentially adequate agency would be a fundamental shift in the character of the metabolic milieu, since the chromosomes, being chemical in nature, are at one and the same time the products of and the contributors to the general type-specific metabolic environment. Note that I write the character, not the degree, for a shift in degree would largely affect the speed and not necessarily the type of reaction.

Now such a shift occurs in conditions of thyroid deficiency. It is therefore possible that the sensitivity of the thyroid to respond by changes in functional level to changes in environment, being continuously brought into play in one direction over long periods of time, might well afford a mechanism through which the inheritance of acquired characters is producible.

The obvious objection to these speculative interpretations is the fact that there are many species of organisms which do not possess a thyroid, and hence what has been written here has but a limited if any significance.

On the other hand it must not be overlooked that the general applicability of the concept is not centered on the thyroid as such but on the thyroid as a factor concerned in the maintenance of the metabolic milieu characteristic of the species possessing the organ. If the basic idea is correct any fundamental distortion of the character of the metabolism (i.e., of its inter-constituental relations) uniform in direction over long periods of time acting through countless generations should be a potentially adequate mechanism whereby varieties within a species, plant or animal, species within a genus, and the inheritance of acquired characters are producible.

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As this goes to press the American Chemical Society's Monograph on *Thyroxine* by Kendall makes its appearance. In this there is to be found the material chosen from the viewpoint of the chemist with respect to the compound designated in the title.

HOW LARGE IS THE MAMMALIAN EGG?

A REVIEW

By CARL G. HARTMAN

Department of Embryology, Carnegie Institution of Washington, Baltimore, Md.

IF ONE sketch the outline of a hen's egg so as to fill a page of this Journal as nearly as possible, the egg of the oviparous Australian mammal *Ornithorhynchus*, drawn to the same scale, would be represented by the natural size of the hen's egg, the entire opossum egg with its albumen, by a cross-section of the lead in a pencil, the human egg by a period in average sized type.

Within the phylum *Vertebrata* the differences between the smallest eggs, those of mammals, and the largest is even greater. Thus the eggs of certain "man-eating" sharks (Lamnids) are as much as 220 mm. in diameter. The egg shell of the now exterminated *Apyornis* measured 350 mm. or over a foot in its longest diameter. The ostrich egg is 150 mm. in length and has a capacity of 1.2 liters, or over a quart.

In the evolution of mammals, the Monotremes (*Ornithorhynchus* and *Echidna*) form an interesting link, for they possess in their hairy covering and milk secreting glands the chief distinguishing class characteristics of mammals. Yet they "lay" large yolk-laden eggs from which the young emerge after a short incubation outside the female's body. From the 15-millimeter egg of *Ornithorhynchus* and the 15-millimeter egg of *Echidna* there is a sudden drop to the typical mammalian egg, which measures about one-tenth of a millimeter. It is true that the marsupial eggs show some transitional characters, as for example, the large albumen layer, the shell membrane, and a somewhat richer supply of yolk, as in *Dasyurus* (Hill). But throughout the *Eutheria*, the mammals above the marsupials, the egg is very uniform, with not much over a two-to-one variation in size (table 8), which holds from rat to man, from bat to horse, from mouse to elephant and whale. The size of the animal bears no relation to the size of the egg.

The comparison between the large yolk-laden eggs on the one hand and the human egg or the eggs of most mammals on the other is not fair to the latter group, for these represent only the yolk or "vitellus" of larger eggs. The total diameter of the hen's egg, for example, is due largely to the albumen laid down in the oviduct around the vitellus. The human egg has no such envelope, and this is true of all mammals with the exception of the marsupials and the Lagomorpha (hares and rabbits). Thus the egg of our only marsupial, the opossum, has a thick albumen layer enclosed in a thin shell membrane; the rabbit egg lacks the shell membrane, while all other mammalian eggs have only a highly transparent limiting membrane, or "zona pellucida," which they receive in the ovary before their discharge into the oviduct. The opossum egg, with its opaque white ovum proper in the center of a transparent, hardly visible albumen sphere, looks, in reflected

light, much like a grain of sago not quite cooked through—a hyaline sphere with a white spherule in the center.

This comparison between the egg of fowl and that of mammals must be controlled in another way. The yolk or vitellus of the hen's egg is so laden with fat and protein pabulum for the developing embryo that the egg nucleus, with its associated tiny mass of protoplasm, which alone will make the chick embryo, becomes all but lost on the surface of the yolk. But that speck of protoplasm corresponds to the entire Eutherian egg. The reduction in size has, of course, been made possible by the parasitic habit assumed by the mammalian fetus through implantation in the maternal tissues.

In order to visualize for himself the actual size of the mammalian egg, the reader may follow the suggestion which the Berlin anatomist Waldeyer was wont to give his students. Spread out, said he, a sample of sand on a sheet of paper, brush off the easily visible grains and pick out the smallest grain, which it is just possible to see with the naked eye—that speck is of the order of magnitude of the mammalian egg.

THE DISCOVERY OF THE MAMMALIAN EGG

In view of the small size of the mammalian egg, it is not at all surprising that it so long escaped detection. It was not until 1827 that von Baer announced the discovery of the real mammalian and human eggs. From the time of de Graaf (1673) to that of von Baer the large vesicular follicle of the ovary was regarded as the egg. We now know that the ovarian follicles that bear de Graaf's name do not constitute the egg but *contain* the egg. The clear, limpid "graafian" follicles in the ovary of the rabbit, before their dehiscence, do greatly resemble eggs of about eight days' development, but how such large eggs were to pass through the narrow lumen of the oviduct did not, it seems, concern many investigators. I read, however, in Ritchie's interesting book, *Contributions to Assist the Study of Ovarian Physiology and Pathology* (1865) that Morgagni, in his *Adversaria Anatomica Omnia* (1741) made the following reflections: "How much more likely is the conjecture that they (the ovarian follicles) are glands secreting fluid for the purpose of keeping the ovum safe, and helping it to escape when the proper time arrives." The error referred to above was a costly one and doubtless retarded progress in the study of embryology during the century preceding von Baer. It is interesting to note that Jones (1837) varied the error of deGraaf by confusing the gelatinous envelope of the rabbit egg with the liquor folliculi.

However, the century following the "Father of Embryology," the nineteenth, did not produce a large array of investigators who occupied themselves with the study of the early stages of the mammalian egg. Without a doubt the outstanding figure was Bischoff, who published, in the forties and following decades, his classical studies on the rabbit, the dog, the guinea-pig, and other domestic animals, as also the deer. These studies have stood the test of time; Bischoff's measurements on the living eggs were the most extensive up to a very recent date.

My calculations of Bischoff's data are uniformly too high. I have followed Keibel's equivalent of 3 Prussian Inches (P.Z.) the equal of 80 mm. This approximates our equivalent of 25 mm. for one inch. Thus the average given for the dog egg (1845, page 7) is 0.0068 to 0.0070 P.Z. or 1/13 to 1/12 P.L. or 16 to 19/100 mm. These dimensions in micra, according to my calculations would be: 181 to 186, 170 to 184, 166 to 190. It seems that Bischoff attempted exactness only in terms of decimal fractions of the P.Z. (preussischer Zoll.). Since his measurements run pretty uniform though high it is probable that the

unit of measurement he used was smaller than he thought by a small fraction.

Sobotta (1895) studied 1459 mouse eggs in maturation and early cleavage, and Long and Mark (1911) 1000 mouse eggs in maturation and fertilization. These constitute the most extensive studies of a single species and on a limited phase of development, but they do not include a single measurement on the living egg. As will be pointed out herein, it is the living egg alone that affords the true picture of the egg as a whole and it is only recently that such studies have gotten under way. This fact does not, however, minimize the fundamental processes in the behavior of the egg which only microscopic preparations can disclose; for stained preparations have taught us about the significant behavior of the chromatin, the chief bearer of hereditary characters.

TABLE 1

From Long and Mark (1911), showing changes in size of the mouse egg during maturation and fertilization, based on eggs fixed in situ

STAGE	NUMBER OF EGGS	AVERAGE DIAMETER IN MICRA
Ovarian:		
Germinal vesicle	109	65.5
Beginning of first maturation division	53	62.5
First maturation division	211	58.0
Tubal:		
Second spindle	507	55.6
Second maturation division	36	53.6
Pronuclei	123	54.0
Eggs in oviduct 16½ hours	50	53.3
Eggs in oviduct 29 hours	50	56.5

SHRINKAGE OF THE TUBAL EGG

Can we state in definite figures, then, with reasonable accuracy, the dimensions of the ovum in each species of mammal thus far studied? Before answering this question we must further define it. In the first place, we must specify the stage of development considered, for manifestly, sooner or later, the egg begins to grow. In this discussion we shall limit ourselves to the one-celled or undivided stage, or at least to the stage of early cleavage. These alone approximate the freshly discharged egg. Now there is considerable evidence in the literature that the nuclear changes of first maturation division in the ovary, the second division, and fertilization after ovulation involve also changes in the size of the egg, even entirely aside from the small mass of cytoplasm and nuclear material extruded with the polar bodies. Long and Mark state that a maximal size of the egg is reached at the end of the so-called period of growth, while the egg nucleus is in the condition of a vesicle. From this time to fertilization there is a progressive slight shrinkage, after which the egg increases in size with its sojourn in the tube. Long and Mark's figures are quoted in Table 1 because they are unique in the number of eggs measured and the care with which the work was done.

TABLE 2

Sizes (in micra) of ovarian and tubal eggs calculated by the present writer from the atlas of van der Stricht (1923) and from his bat paper (1909)

ANIMAL	OVARIAN EGGS	TUBAL EGGS
Man	141×113	
Dog	111×92	102×87
Cat	95×84	81×72
Guinea pig	77×63	63×58
Bat (1923)	95×78	70×65
Bat (1909)	90×69	66×58
Mouse	80×62	53×53

Lams and Doorme (1907) were probably the first to call attention to this phenomenon, which O. Van der Stricht,

their teacher, believed to be quite general for mammalian eggs. This author also believed that the low point varies in different mammals, but in view of the condition of the material on which he made his measurements we may well doubt that so nice a point could have been determined by him. That the ovarian egg is generally reported to be larger than the tubal egg there is no doubt, as one can readily see by a study of the literature. Sobotta in 1905 set down the mouse egg at 59 micra for both the ovarian and the tubal stages, but in a later paper he granted 65 to 70 micra to the ovarian, 60 to the tubal ovum. From Van der Stricht's extensive data I have calculated Table 2, from the standpoint of the present comparison. This author's paper of 1923 constitutes a veritable atlas of the early history of the mammalian egg, based on the most extensive and varied series in the world.

A similar excess in size of ovarian over tubal ova I have reported for the opossum, where, however, the former were measured in situ, the latter after being washed from the tube and studied singly. Other data in the literature were mostly based on material fixed and sectioned, usually in situ. The measurements are thus open to objection; both ovarian and tubal eggs should be studied alive in the same medium. This I have done in the case of the rabbit. Ovarian eggs removed from the right ovary, excised surgically seven hours post coitum, measured on the average 122 x 119 micra. Nineteen hours later two eggs were taken from the left fallopian tube; they were in the two-celled stage when removed, but divided again and were four-celled before they could be photographed. They measured 124 x 124 micra, a little larger than the ovarian eggs. Dr. W. H. Lewis killed a rabbit ten hours post coitum, when some of the eggs had been shed while others were still retained in the follicles. One ovarian egg measured 119, the other 133 micra; the average for tubal ova was 124 micra. The progressive changes in size of the mammalian egg, therefore, await more extensive study. This will be made by better methods in connection with other studies on the egg.

SHRINKAGE DUE TO FIXATION

The size changes incident to the vital activities of the developing egg, as set forth above, become insignificant when compared with the shrinkage caused by fixing agents and the after-treatment used in making microscopic preparations. Hence we must know under what conditions the eggs are measured. Since the introduction, about 1870, of the paraffin method of section cutting, by which an egg one-tenth of a millimeter may readily be cut into ten or more sections of convenient thickness, the tendency to use the method on all occasions has been overdone, for it has been substituted for the older and, for some purposes, better method of studying the object in the living state. Refined technique has often been made an end in itself, rather than an aid. Fixing fluids, too, cause a variable amount of shrinkage, those containing osmic acid the least of all. The rate at which the reagents are changed is another important factor. With the most careful treatment the writer kept the shrinkage down, for the most part, to about 15 per cent; more speed in handling the material would certainly have resulted at times in a 30 per cent shrinkage, which is not unusual in much of the work published on the mammalian egg. The study of the mouse egg might be cited in this connection. Sobotta (1905) gives 59 micra for the average mouse egg fixed in either ovary or tube, but in a later paper states that 65 to

70 micra is nearer the truth for the ovarian egg. Kirkham (1907), basing his measurements on the living egg, gives 80 micra for the ovarian, 73 to 78 for the tubal egg. The writer recently photographed five ovarian eggs of a field mouse (sp. ?) and these averaged 95 micra in diameter. It is therefore evident (and on this point there is no disagreement among the authorities) that the fixed egg is no criterion of normal size of the living, functioning egg.

A further complication is encountered if one attempts to calculate the size of eggs from authors' illustrations where the magnifications are indicated. Articles that fail to indicate magnifications are, of course, of no avail for the purpose of this study (e.g., Rein, Melissinos). Were we to refrain entirely, however, from making calculations from the illustrations in the literature, there would remain jolly little data. The proneness of authors to let the reader make the calculations for himself is illustrated by Van der Stricht's invitation (1923, page 279): "I shall not speak further about the exact dimensions of the eggs [he had not yet given any 'exact dimensions']—it is easy to calculate them from the drawings." This invitation I have accepted, as did Corner (Cowdry's "Special Cytology," volume II, page 1112). The results must, however, fall somewhat short of the true diameter of even the fixed egg, for sections are selected that pass through features of interest, namely the egg nucleus, division spindle, and polar bodies. If these landmarks happen to fall in the middle section of the series the section fairly represents the actual size of the egg; if, on the other hand, the section is a tangential one, the egg is actually larger than the section shows it to be. It is therefore apparent

TABLE 3

Measurements made from photographs of mammalian eggs taken in the living state. Negatives on file at the Carnegie Laboratory of Embryology, Baltimore. Diameter of ovum proper (vitellus) or inner diameter of zona. Dimensions in micra

ANIMAL	STAGE	NUMBER OF EGGS	AVERAGE SIZE	INVESTIGATOR
Rabbit	1–4-celled	6	126	Gregory
	Early cleavage	22	124	Lewis
	Ovarian	1	119	Lewis
	Ovarian	1	133	Lewis
	Ovarian	5	120	Hartman
	2–4-celled	2	124	Hartman
Mouse	Ovarian	5	95	Hartman
Dog	1-celled tubal	3	120	Hartman
Pig	1-celled tubal	4	111	Heuser and Streeter
	Cleavage	8	121	Heuser and Streeter
Opossum 56	1-celled tubal	2	145	Heuser and Hartman
313	1-celled tubal	2	126 x 106	Heuser and Hartman
351	1-celled tubal	11	108 x 100	Heuser and Hartman
336, 337	Cleavage	6	151 x 140	Heuser and Hartman
842	Early tubal	7	157 x 152	Hartman
833	1-celled tubal	2	17?	Hartman
766	Uterine	1	14.	Hartman
Various litters of opossum	Uterine	100	155	Hartman

TABLE 4

Eggs (vitellus only, or inner diameter of zona) measured in prepared sections of fixed ovaries. Sizes in micra

ANIMAL	AUTHORITY	MAXIMUM	MINIMUM	AVERAGE	REMARKS
Dasyurus	Hill, 1911	270 x 260	280 x 126	240	Stated
Didelphis aurita	Hill, 1918	—	—	142 x 129	Stated
Didelphis virg.	Hartman, 1919	185 x 150	—	—	Stated
Armadillo	Newman, 1912	—	—	53	Calculated
Mouse	Sobotta, 1895	—	—	59	Stated
	Sobotta, 1908	70	65	—	Fleming fix., stated
		63	59	—	Bichrom. fix.
	Gerlach, 1906	71 x 55	53	63 x 54	Calculated (few eggs)
	Kirkham, 1907	—	—	71 x 64	Calculated (2 eggs)
	Lams and Doorme, 1907	—	—	68	Osmic fix., stated
		—	—	62	Non-os. fix., stated
	Long and Mark, 1911	77	50	59	Cf. Table 1
	Van der Stricht, 1923	93 x 64	67 x 60	80 x 62	Cf. Table 2
	Kremer, 1924	75 x 75	65 x 55	70 x 70	Calculated
Rat	Kirkham and Burr, 1913	77 x 72	65 x 55	69 x 63	Calculated
	Sobotta and Burckhard, 1910	65	60	—	Stated
	Kremer, 1924	63 x 55	45 x 45	53 x 47	Calculated
Guinea-pig	Rein, 1883	—	—	84	From Lams, 1913
	Lams and Doorme, 1907	—	—	83	Osmic fix., stated
		—	—	79	Non-osmic fix., stated
	Rubaschkin, 1905	92 x 88	80 x 75	89 x 78	Calculated from figures!
		60	55	—	Stated by author!
	Lams, 1913	—	—	80	Fleming fix.; calculated
				70	Non-osmic fix.; calculated
	O. Van der Stricht, 1923	87 x 60	67 x 60	77 x 63	Cf. Table 2
Dog	O. Van der Stricht, 1923	123 x 87	95 x 80	111 x 92	Cf. Table 2
Cat	R. Van der Stricht, 1911	180 x 98	111 x 90	—	2 eggs; calc.
	Longley, 1911	92	79 x 74	—	Calculated
	O. Van der Stricht, 1923	100 x 90	87 x 81	95 x 84	Calculated
Ferret	Robinson, 1918	133 x 116	98	110	Calculated
Horse	Hartman	—	—	135	Carnegie collection (in toto prep.)
Bat	Van Beneden and Julin, 1880	113	90	104	Calculated
	O. Van der Stricht, 1909	110 x 105	50 x 44	95 x 78	Many eggs; calculated
	O. Van der Stricht, 1923	97 x 70	81 x 67	90 x 68	3 eggs; calculated
Human	Nagel, 1888	199 x 194	170 x 165	—	2 eggs (with zona)
	Waldeyer	—	—	130	1 egg
	Bumm (Gynecology)	—	—	200	Stated (with zona)
	Kölliker (Grundriss)	—	—	200	Stated (with zona)
	O. Van der Stricht, 1905	157	120 x 110	140 x 121	Calculated from 13 figs.
	O. Van der Stricht, 1923	179 x 103	107 x 92	141 x 103	Calculated 4 eggs
	Hartman	—	—	120 x 110	1 egg (Carnegie)
Monkey					
(*M. nemestrinus*)	Selenka, 1903	—	—	Ca. 40	Stated
(*M. rhesus*)	Hartman	108 x 100	105 x 90	110 x 93	Carnegie Coll.
Gibbon	Hartman	—	87 x 80	—	1 egg (Carnegie Coll.)
Gorilla	Hartman	—	—	90 x 87	1 egg (Carnegie Coll.)

TABLE 5

Tubal ova studied in sections after fixation, either in situ or after first being removed from the tube. Starred in the latter case. Size in micra (vitellus or true ovum only)*

ANIMAL	AUTHORITY	MAXIMUM	MINIMUM	AVERAGE	REMARKS
Didelphis (opossum)	*Hill, 1918 (*D. aurita*)	170 x 150	112 x 100	126 x 117	Cleavage; calculated
	*Hartman, 1919 (*D. virg.*)	148 x 125	102 x 76	122 x 104	Stated
Hedgehog	*Fischer, A.	46 x 40	—	—	One 3-celled egg; calculated
	Baumeister, 1913	—	—	69 x 54	One egg; calculated
Mole	Heape, 1886	159 (?)	120	125	Calculated
Mouse	Sobotta, 1895, 1898	—	—	59 to 60	Stated
	Lams and Doorme, 1907	—	—	63	Osmic fix.; stated
		—	—	57	Non-osmic fix.; stated
	Gerlach, 1906	68 x 55	48 x 41	60 x 48	Many eggs
	Anikiew, 1908	60 x 58	—	—	Calculated
	Long and Mark, 1911	—	—	55	Cf. Table 1
Rat	Sobotta and Burckhard, 1910	60	55	—	Stated and calculated
	Kirkham and Burr, 1913	67 x 63	55 x 53	61 x 57	Calculated
	Huber, 1915			70 x 62	Few eggs
Guinea-pig	Lams and Doorme, 1907			69	Osmic fix.; stated
				65	Non-osmic fix.; stated
	Rubaschkin, 1905	90 x 74	72 x 58	82 x 67	Calc. from figures × 530
		60	55	—	Stated
	Lams, 1913	60	45	55	Calculated
Rabbit	*Assheton, 1894	145	130	133	Calc. 7 figs. × 165
	*Nihoul, 1926	96 x 92	86 x 80	91 x 83	Calc. Benda fix.
Dog	*O. Van der Stricht, 1923	117 x 103	83 x 70	102 x 87	Calculated; cf. Table 2
Cat	R. Van der Stricht, 1911	114 x 100	89 x 75	105 x 93	Calculated
	Bonnet, 1897	—	—	100	1 egg calc.; Fleming fix.
	Bonnet (text), 1922	—	—	111 x 106	1 egg calc.
	*Longley, 1911	—	—	99 x 81	Calculated
	Hill and Tribe, 1924	90 x 80	69 x 57	82 x 70	Stated
Sheep	*Assheton, 1898	123	105	114	Calculated
Pig	*Assheton, 1898	116	81	100 x 95	Calculated
Deer	Keibel, 1901	115	111 x 106	113 x 108	Calculated
Bat	Van der Stricht, 1909	83 x 73	60	70 x 65	"Selected as typical"
	Van der Stricht, 1923	97 x 70	54 x 53	73 x 62	Cf. Table 2
	Hartman			87 x 73	Carnegie Coll.; 1 egg
Tarsius	Hubrecht, 1902	82 x 70	72	77 x 71	Calculated
Monkey (*M. nemestrinus*)	Selenka, 1903	—	—	40	4-celled

that measurements based on even the best fixed material, especially that fixed in situ, fall short of the actual size of the living egg. This is entirely aside from the irregular shapes which the eggs assume when fixed in situ. I have seldom seen a nicely rounded egg fixed and prepared in the fallopian tube of any animal and I presume that Sobotta had the same experience. Nevertheless this author, by "artistic license," pictures his specimens in what he considered their normal rounded shape. His drawings are the illustrations of maturation, fertilization and cleavage of the mammalian egg most used in the embryological textbooks of all countries.

TABLE 6

Sizes of eggs removed from ovary and measured in living state. Sizes in micra. Vitellus only. (See also Table 3)

ANIMAL	AUTHORITY	MAXIMUM	MINIMUM	AVERAGE	REMARKS
Ornithorhynchus	Gatenby and Hill, 1924	4.4 x 4.16 mm.	—	—	4400 micra
Ornithorhynchus	Caldwell, 1887	2.5 mm.	—	—	2500 micra
Echidna	Caldwell, 1887	3.0 mm.	—	—	3000 micra
Mouse	Kirkham, 1907	—	—	80	
Guinea-pig	Bischoff, 1852	—	—	75	Calc. from figs. × 350
	Reichert, 1861	—	—	87	Calc. from figs. × 320
	Rein, 1883	—	—	65	Calc. from 1 fig.
Rabbit	Bischoff, 1842	182	142	161	Stated (1 P.Z. = 25 mm.)
Dog	Bischoff, 1845	190	166	—	Stated
	Bischoff, 1844	166	160	—	Stated (from polyov. foll.)
Cat	Krause, 1838	170	120	144	Six eggs; calculated
	Longley, 1911	130	105	—	Stated
Goat	Krause, 1838	185	120	—	3 eggs; calculated
Pig	Bischoff, 1844	140	111	—	Several eggs
	Lowery, 1911	157	—	—	"Largest of many"
Bat	Van Beneden and Julin, 1880	—	—	105	1 egg
Macaque	Krause, 1838	140	92	118	3 eggs

THE STUDY OF THE LIVING EGG

What were perhaps the beginnings of a new method in the study of the mammalian egg were made in 1918 by Dr. C. H. Heuser, who, with the writer, under the auspices of the Wistar Institute, made a large collection of opossum eggs at the University of Texas. Many batches of eggs and embryos were at that time photographed in physiological salt solution immediately after removal from the animal. With the assistance of Dr. Heuser, at the Carnegie Laboratory of Embryology, many remarkable photographs of the living rabbit egg in cleavage and germ-layer formation have been secured by Dr. P. W. Gregory and others, and negatives of the early stages of living eggs of other mammals are rapidly accumulating. Indeed, at this laboratory Dr. W. H. Lewis is doing pioneer work in the cinematography of the developing rabbit egg, as he is combining tissue culture with motion picture technique. He has thus far succeeded in keeping the egg alive in rabbit blood plasma for over a week and photographing its normal development for over four days—that is, through cleavage and the formation of the segmentation cavity. The observer may see

the entire process before his eyes in a few minutes and much may be learned which would absolutely escape notice by other methods.

taken in Texas and of the rabbit egg after photographs taken by Dr. Gregory and Dr. Lewis.

This section on the measurement of the

TABLE 7

Tubal ova studied in the living state. Sizes in micra. Measurements of ovum proper or vitellus only, or in a few cases, chiefly early cleavage stages, inner diameter of zona. See also Table 3

ANIMAL	AUTHORITY	MAXIMUM	MINIMUM	AVERAGE	REMARKS
Platypus	Burrell, 1927	3.0 mm.	—	—	Whole egg 17 x 14 mm.
Echidna	Simon, 1894	—	—	—	Whole egg 16 x 13 mm.
Dasyurus	Hill, 1911	300 x 290	—	250 x 240	Stated
Opossum	Hartman, 1919	157 x 152	108 x 100	130 x 123	Stated
Hedgehog	Keibel, 1888	120	—	110	(In toto in OsO_4); stated
Mouse	Kirkham, 1907	78	73	—	Stated
Rat	Bischoff, 1844	—	—	100	One egg; stated
	Kirkham and Burr, 1913	—	—	79	Stated
Guinea-pig	Bischoff, 1852	106	91	—	Stated (3 P.Z. = 80 mm.)
	Bischoff, 1852	74	70	72	Calc. from figs. × 350
	Bischoff, 1852	—	—	75	After Lams
	Reichert, 1861	—	—	87	After Lams
	Hensen, 1876	82	65	75	Calc. from sev. eggs
Rabbit	Bischoff, 1842	180	139	160	Stated.
	Costl, 1834–1849	—	—	120	Calculated
	Hensen, 1876	—	—	103 x 93	Calc., 1 fig.
	Grèwsdew, 1896	144	120	133	Calc., sev. figs.
Dog	v. Baer, 1827	—	—	144	"1/15 of a line"
	Bischoff, 1845	174	125	145	"3 P.Z. = 80 mm."
	Hartman	—	—	120	Carnegie Coll.
Cat	Longley, 1911				Cf. Table 3
	Hill and Tribe, 1924	153 x 136	119 x 110	130 x 119	6 eggs in osmic fix.
Sheep	Bischoff, 1844	—	—	140	1 egg; stated
Deer	Bischoff, 1854			115	Stated
Pig	Corner and Amsbaugh, 1917	145	135	140	14 eggs, 3 litters
	Heuser and Streeter, 1928	131	116	121	10 eggs, 3 litters
Bats (spp.)	Van Beneden, 1911	95	86	91	2 eggs (118, 108 with zona)
Monkey	Corner, 1923	86	83	—	2 eggs, degenerating
	Allen, 1927	104	87	—	2 eggs, degen.
	Allen, 1928			104	1 egg, degen.
	Hartman	—	—	107	1 egg, degen.
Human	Allen, *et al.*, 1928	184	117	132	With zona

Photography thus applied to embryology may therefore be expected to yield valuable results. Certainly, from negatives the size of the eggs may be calculated at one's leisure. In Table 3 I have given a number of measurements, chiefly of the opossum egg after photographs

living egg must not be closed without mention of an event of the greatest significance; namely, the discovery of the first human tubal ovum by Edgar Allen and associated surgeons (Dr. Pratt of Detroit and Drs. Newell and Bland of St. Louis). Seven eggs were recovered from

TABLE 8

Interpretive table, giving the reviewer's estimate of the true average size of the egg of various species of mammal thus far studied. Studies on the living egg are considered the more authoritative and due correction is made for data based on fixed eggs. Dimension of vitellus only. Jenkinson (1913) probably gives size of entire egg

ANIMAL	MOST PROBABLE SIZE OF EGG IN MICRA	JENKINSON'S TABLE
Monotremata		
Platypus	2.5 mm.	
Echidna	3.0 mm.	
Marsupialia		
Dasyurus	240	280
Didelphis	140–160	130
Edentata		
Armadillo	80	
Cetacea		
Whales	140	
Insectivora		
Mole (Talpa)	125	90
Hedgehog (Erinaceus)	100	60
Rodentia		
Mouse	70–75	60
Rat	70–75	
Guinea pig	75–85	80
Lagomorpha		
Rabbit	120–130	150
Carnivora		
Dog	135–145	180
Cat	120–130	
Ferret	120	
Ungulata		
Horse	135	
Sheep	120	150
Goat	140	
Pig	120–140	
Cheiroptera		
Bat	95–105	
Lemurs		
Tarsius	90	
Primates		
Gibbon	110–120	
M. rhesus	110–120	
Gorilla	130–140	
Man	130–140	

six women. The measurements were made on the fresh eggs and are given in Table 7. Previously Corner (1923) and Allen (1927) had recovered eggs from the monkey. These were also measured before fixation (Table 7). The egg of *Macacus nemestrinus*, in the four-celled stage, was studied by Selenka (1903) in the fixed tube and measured in the shrunken state only 40 micra. These cases mark the beginning of the study of the earliest tubal ova in Primates.

THE SIZE OF THE MAMMALIAN EGG

We now return to the original question, How large is the mammalian egg? The reflections set down in this review force the conclusion that for no species of mammal is there agreement on measurements of the egg. Those reported have a range far in excess of variations in the normal living egg, great as these variations undoubtedly are. Perhaps the smallest and the largest of a given species, that is, the extremes in size range of living eggs, are not viable. But we know nothing about this problem; it is one that only tissue-culture methods can solve. The reviewer has therefore thought it desirable to bring together the data contained in the world's literature (at least in that major portion available to him) on the size of the mammalian egg and to present it for what it is worth. If the figures are unsatisfactory the study will serve to emphasize the need of further work and more careful methods than those employed in respect to the making of measurements in the past. For the convenience of the reader the data have been condensed into Tables 4, 5, 6 and 7, classified according to the headings of the tables. As a summary of the whole the writer has been bold enough tentatively to put down in Table 8 his own ideas as to the normal range of the average or modal egg size for the various species of mammals. The table is based first on the best measure-

ments of the living egg and second on an evaluation of the data given by the various authors, due correction being made for the methods used. The table should, however, be regarded merely as a basis for revision in the future. Nevertheless, a perusal of the figures will show that Van der Stricht was probably right when he stated the human egg to be the largest, that of Muridae the smallest among the mammiferous animals. It is also apparent that the smallest eggs are probably not as small as the former estimates would have them, the largest not as large as previously stated. The mouse egg is nearer 70 than 50 micra, the human egg nearer 150 than 200. In other words the table has a tendency to level up the differences in the sizes of mammalian eggs.

Finally it is hoped that the appended literature list will prove helpful to those studying the mammalian ovum for the first time. Studies on the ovum just before and just after its discharge from the ovary were, of course, considered the essential studies. Others might have been added which give sizes of the ovarian egg incidental to histological studies on the ovaries; but it is believed that the list includes a sufficient number of these. The list of papers and books on tubal ova, practically all of which have been consulted by the writer, is believed to be fairly complete.

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SYSTEMATIC BIOLOGY AND THE MUTATION THEORY

By G. F. FERRIS

Department of Zoölogy, Stanford University

THERE are certain phases of biological investigation which begin with an inquiry into the numbers and the distinguishing characteristics of the different kinds of plants and animals. They continue with an attempt to arrange these kinds of organisms into a classificatory system. They end with an attempt to apply the data thus accumulated to various problems, some of which may be approached only by this very round-about method. All of these activities may be grouped under the general term of "Systematic Biology."

The older theories concerning the processes of evolution were very largely the product of the activities of those who were wholly or in part systematists—witness Darwin's monograph of the Cirripedia—or whose thinking was of the type peculiar to those trained in that particular school. The current theories are increasingly the product of those who are primarily of the experimental or physiological schools and these in their turn are already beginning to give way to those who are primarily chemists.

With such differences in background it is inevitable that there should be differences in the conclusions to which the members of these various groups are led. These conclusions come at times quite sharply into conflict. Matters which from the point of view of one group may seem quite simple become, from the point of view of another, extremely dubious, with such simplicity as they may appear to possess ascribable rather to the minds of those holding the opposite view.

These differences of opinion are perhaps most sharply marked in connection with one particular problem, that of the method of evolution. There are doubtless those among the most modern of all biological groups—the biochemists and the biophysicists—who will not hesitate to yawn audibly at the mention of this problem, just as members of the somewhat less modern groups of experimentalists and geneticists are prone to indicate their boredom with the systematist who talks about "species." It may very well be that all of our speculation as to the mode of evolution is fruitless and that eventually it will rest with the colloid chemist to tell us whether evolution is even a physical possibility and if so how it can have come about.

Pending that time, however, there are still biologists who are interested in speculating about this problem, and its literature grows at a rapid pace. The matters that I wish to discuss here are little side issues of this major problem and have to do with some questions that have arisen concerning the validity of certain assumptions upon which systematists, consciously or unconsciously, base their conclusions. Systematists in the

past have contributed to the development of the theory of evolution. In turn that development has influenced the work of systematists. It is proper to inquire what the reaction of the newer theories upon the work of the systematist may be. It is proper to inquire into the basic assumptions of such work and to speculate on the question of whether they check with these newer theories. If not, it is also proper to speculate upon the meaning of the discrepancies.

THE ASSUMPTION THAT CLASSIFICATION EXPRESSES PHYLOGENY

In the pre-Darwinian period, as has many times been pointed out, systematic biology rested upon certain assumptions which are now discarded. It was assumed—quite automatically and almost certainly without any thought that an assumption was being made—that all the species of organisms had been created at one time and that they had remained fixed and immutable since that time. Consequently the "species" was a perfectly fixed and definite thing. It was an actual entity, capable of being placed in a definite pigeon-hole where it would for all time rest in peace and comfort. On this basis, classification, or the attempt to arrange these species into some sort of system, could be nothing more than an attempt to express degree of apparent resemblance. To it there could be attached no deeper significance.

But with the general acceptance of the theory of evolution this condition changed, although it so happened that the nomenclatorial mechanism that had been developed under the previous régime remained to do duty under the new, thus giving some semblance of continuity between the two opposing ways of thought. If species evolve, if they change one into another, then they can no longer be placed in such pigeon-holes, or if they are so placed they may not long be permitted to rest in peace. They must recurringly be dragged out of their repose and bedeviled with questions as to their claims for recognition. Particularly will this be true if evolution has actually taken place by way of a gradual molding of one species into another by means of slow and cumulative changes.

Necessarily the philosophy of classification changed at the same time. Theoretically at least it became something more than an attempt to express merely degrees of resemblance. It became an attempt to express phylogeny, to record the history of evolutionary development. The various taxonomic categories have been assumed to indicate degrees of "blood relationship." This assumption expresses itself graphically in the familiar "family trees."

All of this in theory. Actually, perhaps, the work of systematists has conformed in but a small measure to this theory. Morgan (3, p. 43) remarks,

> A few students of the subject still attempt to arrange their species in such a way as to indicate their relationship by descent, but the attempt, while desirable from the standpoint of evolution, has proven so difficult that it has been tacitly abandoned or ignored by many taxonomists.

And Hall (2, p. 4) has said, "It must be admitted, however, that the spirit of phylogeny is not evident in a large proportion of the revisions and monographs of the present day." After all, only a small proportion of the workers in any particular field are likely to be philosophically inclined. The majority are content, perhaps necessarily so, to perform the task immediately before them without considering its philosophical implications, thus undoubtedly saving themselves from a large amount of worry. Certainly the majority of systematists have been con-

tent to name species without troubling themselves very much about the question of whether their "species" were an expression of a definite biological fact or merely of a variable subjective concept. And they have proceeded to group these "species" into genera—or increasingly to isolate them into monotypic genera—and to unite these genera into larger groups without pondering very deeply as to whether they were expressing their phylogeny or were merely putting them together because they look more or less alike.

That the problem bristles with difficulties can not be denied. Consequently it is not to be expected that attempts to reconstruct the phylogeny of any group will be correct in anything more than a broad way. It would obviously be impossible to say of any particular organism, either fossil or living, that it was the actual ancestor of any other organism or group of organisms unless we actually had observed the birth. Lacking such observation we can at the best merely say that there is a strong family resemblance which indicates a probable connection.

Furthermore, even if we had the actual evidence which is necessary positively to demonstrate the phylogeny of all organisms we should still not be free from our difficulties.

If evolution has really taken place by any of the methods which seem at all acceptable, then the number of steps involved in the racial history of any organism from the beginning of life to the present time must be almost infinite. And with a knowledge of those steps we should still have the problem of condensing this history into the limits of a usable classificatory system. The mere mechanical problem of devising such a system would not be small. The degree of compression and distortion which would result might easily be so great as to obscure the facts. Like the so-called "biogenetic law" with its assumption of the compression of the racial history into the embryonic life of the individual, the best that might be said is that some times it seems to have a certain significance.

Nevertheless, if systematic biology is to hold fast to any sort of basic philosophy it would seem that it must hold fast to this. Without at the least the hope that it may express some deeply underlying truth it becomes reduced merely to the accumulation of disconnected and irrelevant facts. That much of systematic work is indeed nothing more than this may, unfortunately, be true, but this does not necessarily imply that there are no other possibilities.

THE ASSUMPTION THAT CLASSIFICATION EXPRESSES DEGREE OF RELATIONSHIP

If we assume that the systematist is attempting to chart the course over which an organism has come during the unfolding of its racial history we may—or at least do—assume that the various categories of our system express also the varying degrees of relationship of this organism to others. Such an assumption is generally accepted by systematists as more or less an axiom.

Let us consider what is meant by the term "relationship" as it is used in such a connection.

In ordinary practice we consider individuals to be related to each other if they have had a common somatic ancestry and we measure the degree of their relationship by the *number of generations* that have intervened between these individuals and the point at which their ancestries merged into a common soma.

As the term is used in systematic biology there is also something of this implication of eventual merging into a common soma, although with modifications. Whether

the "ancestor" involved was an individual or pair of individuals or whether it was a group of individuals—a species—would depend upon whatever theory as to speciogenesis we might adopt. And however that may be, there is the further difference that relationship is not measureable by the number of generations that have elapsed. Except in the case of the pedigreed stock of the geneticist, we know nothing whatsoever of the number of generations that have intervened between any two points and consequently the systematist can not be thinking of any such matter when he speaks of the relationship of two groups.

That this is so can be made perfectly clear. We have at the present time living Brachiopods belonging to a group that originated at least as early as the Paleozoic, but which have come down to us practically unchanged from that time. We speak of these as "closely related" to the fossil forms of the Paleozoic. The mammals presumably originated in the Mesozoic, but the mammals of today are very different from any of the earliest members of the group and are consequently not regarded as closely related to any of these ancestral forms. Yet the difference in number of generations intervening between the present day members of the two groups must be inconceivably great.

Evidently then "degree of relationship," as understood by the systematist, means only the degree to which there is a common possession of anatomical characters and the degree of development of those characters. Thus, those forms which agree in the common possession of a notochord are assumed, regardless of time of origin or number of generations involved, to be more closely related to each other than to those forms which do not possess a notochord. And further, those forms which have the notochord developed in similar degree are considered to be more closely related than those which have it developed in some other degree.

It appears then that while our classification—assuming it to be a true expression of fact—may actually give an indication of the course of evolution, its attempt at expressing degree of relationship is still nothing more than an attempt at expressing degree of difference. Degree of difference and degree of relationship are on this basis synonymous, assuming, of course, that difference is taken to mean actually fundamental difference, such as is determinable by the study of homologies.

But there is another method of approach to this question of relationship.

If we accept the theory of the "continuity of the germ plasm" the soma becomes in a way a secondary development. That which is important is not the house that the germ plasm builds over itself for its own protection but the germ plasm itself. It is the germ plasm alone that constitutes the unbroken stream of life which has come down to us from the very beginning—if there ever was a beginning. The soma, which is discarded with each generation and built up again, can be merely an index to the conditions that exist within the germ plasm. It is only as changes occur within this germ plasm that somatic differentiation—at least differentiation that may be passed from one generation to another—may appear.

Why then, if we are to take the trouble to speculate at all, should we concern ourselves especially with the modifications of the soma except in so far as they are the visible evidence of the make-up of the germ plasm? Theoretically we should define our concept of relationship not in

terms of the evanescent and discontinuous soma but in terms of the enduring germ plasm.

If we approach the matter of relationship from this point of view we arrive at results which are somewhat different from those obtained by a consideration merely of the soma. Phylogenetic relationship comes to mean the convergence of the lines of modification of the germ plasm and degree of relationship is to be measured by degree of germinal differentiation.

It may at first glance appear that after all we have come out by the same door wherein we went. Perhaps for practical purposes that is true, but for the moment we are not concerned with such purposes. Theoretically there may at times be a noticeable difference. It might very well be possible for two organisms to be quite similar somatically and yet quite widely separated genetically, or quite different somatically and yet quite closely related genetically.

Morgan (3, p. 46) has remarked,

> That the visible structural differences between groups of individuals is not a safe guide on which to construct a real distinction (between species), is exemplified by numerous cases in which groups may exist side by side that are so closely similar that only an expert can separate them, yet are either infertile when crossed or else leave offspring that are sterile.

And he cites as a specific example the case of two species of *Drosophila*. Here there is evidently a very considerable genetic difference which is expressed in a very slight somatic difference.

Another example of the difference between the genetic approach to the question of relationship and the usual approach may be found in the case of any hybrid. Let us consider the often told story of the Andalusian fowl, which is to be found as a stock example in almost any book on genetics (3, p. 60). These bluish colored fowls do not breed true, but produce white, blue and black offspring. The white individuals bred among themselves will produce white and the black bred among themselves will produce black.

How are we to consider the matter of relationship in such a case? The answer may have no direct bearing upon problems of systematics, but it will serve to emphasize a point.

On the basis of ordinary usage these forms, having been together in a common soma at one point of their history, are related one to another. But genetically it can hardly be said that such is the case. Genetically they happen merely to have resided for a time within the same house. The white fowls are related—that is are genetically continuous with—the original white fowl which entered the cross that produced the Andalusian, and the black fowls are related to the original black fowl. Genetically they are not related to each other at all, except through the germinal line which leads back presumably to the point where the germ plasms of all fowls merge in a common center. It is evident that conclusions as to relationship which are not checked by genetic tests would lead to erroneous results, or at least to results of differing significance.

Let us consider also the effect of mutations upon our idea that our classification, which is based upon degree of difference, is a measure of degree of relationship.

Let us assume that among the offspring of a single pair of organisms there occur a number of mutants. Somatically they have all come from a common source and would be regarded as equally related. But let us suppose that one individual is a mutant in regard to a single character, another in regard to two, another three, another four and so on. These mutations

may be of quite different orders, some minute, some very conspicuous, as conspicuous, let us say, as the loss of wings in a fly. Let us assume them to breed true so that a line is established. What are we to say of these lines and their relationships?

If degree of somatic differentiation be regarded as our measure, that form which departs most conspicuously and obviously from the parent stock would be regarded as the most widely separated from it. Genetically, however, it would appear that the form which departs in regard to the largest number of genes that have been modified would be the most remote, although it might actually resemble the parent stock the most closely of all.

There is then very clearly a possible difference between degree of relationship as based upon somatic differentiation and as based upon the genetic concept.

The systematist, relying, as he usually must, upon the former for the greater part of his conclusions, is possibly building his house upon the sands. He may not be able to do otherwise, for there may be no other foundation material available in significant quantities and he will simply have to take his chances that his entire structure will some time be swept away by the rising flood of some other method of thought.

Thus far systematists in general have been but little disturbed by fears of such an inundation. As a geneticist once remarked, "Systematic literature grows precisely as if the genetical discoveries had never been made. . . ." Nor can one whose associations are chiefly with systematists have failed to observe that in general they are more or less inclined not to take the work of the geneticists seriously as far as it may have any bearing upon their own conclusions. They have referred even to "the querulities of geneticists and other experimental biologists towards systematic work." Such an attitude, however, can probably not be successfully maintained for long. Whatever apparent differences there may be must in the end be harmonized. Questions raised by investigations in one field may not indefinitely be ignored by workers in another.

THE REACTION OF THE MUTATION THEORY UPON SYSTEMATICS

The particular question that I am here concerned with arises out of the work that has been done, chiefly during the last twenty-five years, on the subject of mutation and its rôle in evolution. And I am concerned with this only as it reacts upon the philosophy of systematic work.

If we accept the theory that mutation has been the dominant, if not the sole, factor in evolution we must be prepared to accept also certain possibilities that appear to be contained within its scope. We must accept, for one thing, the possibility that in some cases mutations of wide extent have taken place. Just how wide that extent may be we do not know. For one thing, changes of too great an order may possibly result in such profound physiological disturbances in the individual that death results. Such would be the case with certain of the types of monsters that occur among human offspring, so malformed that they can not live, but which, if they could live and find an opportunity to reproduce, might conceivably behave as any other mutant. We can not even surmise, then, what the upper limits may be, for we have no way of knowing just what the physiological effect of a change will be. Who can say just what constitutes a "large change?" We do not know, for example, that the physiological processes involved in the complete loss of wings in a mutant of

Drosophila are necessarily much greater than those involved merely in a shortening of the wing.

Again, assuming that a mutant of what we—in the absence of a knowledge of the extent of physiological change—would call marked degree is able merely to survive it may not leave descendants. As Morgan (3, p. 37) has pointed out, "Many, probably most, of the extreme mutant types could not compete with the native types from which they have sprung..." Consequently, there is probably some actual limit to what mutations may do, from the point of view of possibility of survival alone.

Again, it is evident that there are certain things which mutation at least has not done. In spite of the fact that hexadactyly is not an uncommon occurrence in man at least and apparently has no special survival significance, there does not exist any species of six-toed mammal. In spite of the fact that hundreds of thousands of kinds of insects are known in which there is a great variability of the structure of the tarsus, there is no known insect that has a tarsus of more than five segments, although it would seem that a six-segmented tarsus would be no more of a handicap than one of five segments. Innumerable cases of such limits could be cited. It seems that there are some limits beyond which the changes can not go.

Nevertheless, we must be prepared to accept the possibility that evolution by steps of considerable apparent degree has taken place. If this be true we are confronted by a definite problem having to do with the effect of such possible discontinuity upon the theory of systematic work.

Let us revert to the statement that degree of morphological differentiation is accepted by systematists as the measure of degree of phylogenetic relationship. Let us then assume that we have at hand a series of flies, which on the basis of the sum total of their characteristics appear to be closely related, and that of these flies some are fully winged, some have wings of varying length and one is wingless. Preoccupied with the idea that *degree of difference* is significant the systematist would undoubtedly arrange these flies in a series, beginning with the long winged form and proceeding to the wingless form by way of the series of intermediates. He would almost certainly assume that such is actually a phylogenetic series.

And yet the work of Morgan and others on *Drosophila*, where exactly this situation occurs, does not support any such assumption. Morgan (3, p. 20) speaking of this very matter, and of the appearance of other series of mutations in the cultures of this insect, points out that, "The order in which these mutations occurred bears no relation to their size; each originated independently from the wild type."

This being the case, he proceeds to put the inevitable question.

> Suppose that evolution "in the open" had taken place in the same way by means of discontinuous variation. What value then would the evidence from comparative anatomy have in so far as it is based upon a continuous series of variants of any organ?

He is here considering the matter of the evidence for evolution, but inasmuch as all of our systematic theory is based upon the idea of evolution and our systems of classification are merely attempts to summarize the results of its operation, the systematist may take the question as applying directly to his own efforts. If evolution has indeed taken place in this fashion what validity have our labored attempts to express phylogeny and our belief that degree of morphological differentiation is correlated with degree of phylogenetic relationship?

Here is a question that the philosophically inclined systematist has need to ponder.

It would seem quite clear that if species actually arise by such markedly discontinuous steps as those which have been observed and recorded by the geneticists—and with an entirely unknown upper limit of their possibilities—any thought that degree of somatic differentiation has anything to do with degree of relationship must be abandoned. The systematist, under these conditions, would find himself back in the pre-evolutionary period, where all he could hope to do would be to group organisms together solely on the basis of convenience and without any attempt to express any underlying principles whatsoever.

For if mutations of this order are the basis of the origin of species, that is, are the basis of differentiation, we obviously can not say of a series of species that this is most closely related to that and is more remote from another except on the basis of a genetic analysis which will demonstrate how many factors have been involved in producing the differences. But species are grouped together to compose progressively larger categories, each of which presumably represents something of an evolutionary step. Consequently if we cannot depend at all upon our judgment concerning species, how may we dare to hope that our judgment of the larger groups which are composed of species can be any better?

Our whole body of systematic theory, in fact, is built up on the idea of continuity. If that continuity actually does not exist our body of theory falls apart.

We have, however, a curiously paradoxical situation. At the one end of the series apparently we may not trust the evidence. But if we begin at the other end the matter is different. Probably any biologist, regardless of the school to which he belongs, will admit that the vertebrates are more closely related to each other than to any other kinds of animals, and that regardless of the criteria of relationship that may be adopted. Probably also it will be admitted that the mammals are more closely related to each other than to the other vertebrates. And of the mammals it will certainly be admitted that the primates are more closely related to each other than to other mammals. But if the species of primates have arisen by markedly discontinuous mutations we cannot rely upon conclusions as to their relationships within the group.

Where then do we become wrong as we go down the scale or right as we go up it? If marked discontinuity has been at work it would seem that at some point we must inevitably go astray.

Morgan himself (3, p. 22) has given an answer to his own question that is partially satisfactory. It is this, ". . . . our inference concerning the common descent of two or more species is based on the totality of such resemblances that still remain in large part after each change has taken place." But it seems that this answer can not be wholly satisfactory if evolution has actually taken place by steps of great discontinuity.

There is no reason to assume that such discontinuity must be confined to any one organ or part of the body. Evolution has involved every organ. Now, if in an insect, for example, a single step robs the animal of its wings or alters them profoundly, and another step changes the segmentation of the tarsi, and a third changes the antennae, a fourth the genitalia and so on, we come very quickly to a form that can not by the sum total of its characters or in any other way be related to any other. It seems reasonable to suppose that eventually we should arrive

at a condition where all semblance of continuity is lost.

And yet on the whole we do find continuity of a sort. On the whole it is possible to group organisms together so definitely and to determine so clearly the series of steps by which one form may have arisen from another that we have a very strong argument against a belief in such a procedure. It is perfectly true that there are gaps and it is possible that these gaps are an expression of an actual interruption of continuity in evolutionary history. The existence of these gaps has so impressed at least one recent writer (1) that he seems almost to have fallen back upon the idea of special creation as a means of accounting for them.

His statement seems to the present writer curiously inconsistent. He concludes (1, p. 539) "There is not the slightest evidence that any one of the major groups arose from any other. Each is a special animal complex related, more or less closely, to all the rest, and appearing, therefore, as a special and distinct creation." We may pertinently ask at this point, why under such conditions the word *related* should have been used at all.

Yet even this author agrees as to the general picture of continuity. "But within each major group," he goes on to say, "we see a different picture. Here the fossil record shows a constant change from one horizon to another." And of the rise of the reptiles and the mammals, "Here we can trace the gradual development from comparatively insignificant beginnings to a wonderful flowering of specialization and perfection."

Even so, he is still impressed by the amount of discontinuity that can be detected.

But it is well to emphasize that every evolutionary line has certain gaps; some have these gaps large and broad, while in others (as in the horses) the gaps are relatively small. These gaps probably are largely natural, and not due to a deficiency in the record. They indicate the continuation of the phylogenetic line through variants showing a more or less wide departure from the normal type which happened best to meet the conditions of the time.

It is true that some of the gaps are very impressive. Certainly no one has yet been able to devise a theory of the origin of the vertebrates that is satisfactory to everyone, even the apparently careful and profound work of Gaskell having fared none too well. But it seems hardly time yet to abandon utterly all belief in an orderly and regular mode of origin of these larger groups. We may still legitimately cling to the belief that the gaps are due to other factors. There is still the inadequacy of the paleontological record, there is still the fact that after all our knowledge is really very inadequate. The last factor, I think, is not often given the importance that it deserves. It is a quite tenable hypothesis that where an anomalous condition appears in systematic work and its derivatives the most probable explanation is either that someone has made a mistake or that there remain facts still to be discovered. There is no reason to fall back upon an improbable explanation as long as a probable one is at all available.

It will be difficult to convince the systematist in general that evolution has not been in the main a relatively continuous procedure. Such is the conclusion to which a paleontologist—and a paleontologist is merely a systematist—has come. Osborn (4, p. 40) has expressed the view that "Mutation is an abnormal and irregular mode of origin, which while not infrequently occurring in nature is not essentially an adaptive process; it is, rather, a disturbance of the regular course of speciation." This is one possible answer to the question. That it is a satisfactory answer may be doubted.

However, this is not all of the story. No mutationist, probably, will maintain that all evolution has taken place by changes of the order to which we have called attention. In fact the tendency of their thinking seems to be in the opposite direction, and some of them would probably by among the first to point out that any such conception of mutation as we have been discussing is unutterably crude. Morgan (3, p. 130) remarks,

> . . . . even the smallest changes that add to or subtract from a part in the *smallest measureable degree* [the italics are the present writer's] may also arise by mutation. We identify these smaller mutational changes as the most probable variants that make a theory of evolution possible, both because they do transcend the original types and because they are inherited.

This is a very different picture from that suggested by the question which Morgan propounded and which we have quoted. In fact this concept of mutation brings us for all practical purposes back to the original point from which the systematist has begun his theorizing. There remains nothing but a difference in terminology and even that difference can be disposed of. To make clear the nature of this reconciliation, let us consider the meaning of the word "discontinuous."

THE MEANING OF DISCONTINUITY

If we write the numbers 1–2–3–4–5–6–7–8–9–10 we are prone to speak of this as a continuous series. As a matter of fact it is not. It is merely a regular series, increasing by a fixed increment at each step. Actually, from the point of view of one who might be accustomed to dealing with very small fractions it is highly discontinuous, for there is a very large break between each two members of the series.

Again even if we take the series .001–.002–.003 and so on, the mere fact that we have reduced the amounts dealt with does not make the series any the less discontinuous. There is still a break between each two members. So with any fractional series that we may propose. As long as the difference between each two members of the series is measurable the series is discontinuous. The best that can be said of it is that it is regular and orderly.

Now as a matter of fact there can be no such thing as *continuous* variation in organisms. Always between soma and soma there must by the very nature of things be a break. Any measurable difference between successive members of a genetic series constitutes a discontinuity. If that discontinuity be very small and if it be a part of a regular series, especially if that series be cumulative, we would be prone to talk of continuity and it is only in this fashion that we can do so.

Again, if we write the series 1–2–3–4–7–8–10–13–15–16–20, we can not say that this series is either continuous or regular, but we can still detect in it a certain order which leads us to believe that it is a part of a regular progression which has been partially obscured by the presence of gaps.

It would seem that very probably the course of evolution has been something of this sort. Assuming that there actually has been cumulative change—progressive evolution—and I doubt that anyone can successfully argue that there has not, it would probably be something of this type. That is, it seems unreasonable to suppose that if the trunk of the elephant actually arose by cumulative changes those changes were necessarily an inch or five tenths of an inch or three inches at each time. The series may be interrupted, the steps may vary in size, but if we have before us a sufficiently large part of the series we can still trace its course and see something

of how we have come from one extremity to the other.

Consequently, if the mutationist is willing to allow the smallest measureable, heritable changes to come within the meaning of the term "mutation" and is willing to accept the view that on the whole small changes and not those of great degree have been the principal factor in evolution, the difficulties largely disappear. Under such conditions a phylogenetic series, while possibly interrupted and irregular, may still retain enough of the evidence to show the general system upon which it has proceeded from one point to another. The accuracy with which such an interrupted series may be interpreted will vary with the extent of the interruptions and irregularities, and there may actually exist series which will not permit of interpretation. Still it would be reasonable to suppose that our hope of expressing phylogeny will not be entirely unjustified.

And if the systematist can not properly expect an absolute continuity, but must be content only with such a degree of apparent continuity as comes within the lower limits that the mutationist is willing to accept, there would seem to be no special room for argument. There may still remain the possibility that in some cases the systematist working purely from a morphological basis may be misled, but the probability of such occurrences would not appear sufficiently great to be generally disturbing. There remains the desirability that the systematist acquaint himself with the geneticist's contributions to biological theory and that wherever possible he test his results by genetical methods. But there would seem to be no fundamental and necessary conflict.

CONCLUSIONS

Certain rather definite conclusions may be drawn from all this as to the bearing of mutational theory upon systematic biology.

1. The possibility must always be recognized that mutations involving a wide departure from the parent stock may take place and that such mutations may have an evolutionary influence.

2. To the extent that such mutations do occur and become perpetuated, the systematist's conclusions that degree of morphological differentiation may be relied upon as a measure of relationship and as an indication of phylogeny would seem to be invalidated.

3. There is on the whole a great deal of evidence against the theory that such mutations have been the principal factor in evolution. The mutationists themselves do not rest their theory upon them. Admitting that they do occur, they will not necessarily lead to such a degree of discontinuity as to affect the sum total of all characters of an organism so greatly that all traces of relationship are lost, although this might possibly be the result.

4. If minute mutational changes be accepted as the most probable basis for evolution, there would seem to be no special conflict between the mutation theory and the demands of the systematist for continuity.

5. This being the case it would seem that in general the mutation theory does not necessarily invalidate in any large degree the basic theories upon which systematists have been accustomed to rely, although it may require of them some modification and it does require the testing of their results by genetical methods wherever possible.

LIST OF LITERATURE

There seems to be but little literature bearing directly upon the problems here considered. It would obviously be impractical to attempt any bibliography of the general literature of evolution, which furnishes the back-ground. Consequently only those papers which have been quoted in the preceding article are here listed.

(1) Clark, A. H. 1928. Animal evolution. Quarterly Review of Biology, 3: 523–541.

(2) Hall, H. M. 1928. The genus Haplopappus. A phylogenetic study in the Compositae. Carnegie Institution of Washington, Publ. 389: 391 pp.

(3) Morgan, T. H. 1925. Evolution and Genetics. Princeton Univ. Press.

(4) Osborn, H. F. 1927. The origin of species, V: speciation and mutation. American Naturalist, 61: 5–42.

EFFECT OF CLIMATIC FACTORS ON SUCTION FORCE

By TSI-TUNG LI

Nankai University, Tien-tsin, China

I. INTRODUCTION

1. *What is suction force?*

IT IS a well known phenomenon that the water absorption in the root hair from the soil, or in the mesophyll cell from the vessel, has an intimate relation with the osmotic pressure of the cell sap of these cells. Botanists interested in the absorption phenomenon turned their attention to the study of the osmotic pressure of the cell sap of various tissues of different plants. The ordinary method used is what is generally known as the plasmolytic method. It only gives the value of osmotic pressure of the cell sap at incipient plasmolysis, but not at the normal condition. A second method generally used is Beckmann's method of cryoscopy. It involves the determination of the freezing point of the cell sap. This method is more direct and avoids the objection applicable to the first method. But sap extraction involves great technical difficulties. It may introduce a considerable amount of error. Even if we take for granted that the osmotic pressure determination is of sufficient accuracy, the value so obtained tells us very little about the water absorption power at the condition of determination. For the inflow of water into a cell is determined both by osmotic pressure of the cell sap and also by the tension of the elastic cell wall. So the effective force available for water absorption or suction is not the same as the osmotic pressure of the cell sap. This point has been made very clear in Ursprung and Blum's (11) first paper on suction force. According to Ursprung and Blum the available force is a resultant of two component forces: on one hand, the osmotic pressure of the cell sap, which causes the inflow of water, and, on the other hand, the tension of the cell wall or the wall pressure, which checks the inflow of water. The effective force available for suction is termed suction force. Shull (5), however, thought that suction tension is a better term. It can be stated in a simple equation.

Suction force = Osmotic pressure − Wall pressure or

$$S = O - W$$

It is interesting to find out how these three factors react on each other under various conditions.

I. The cell is placed in distilled water. Water is absorbed due to suction force. The cell volume increases. The tension of the cell wall or wall pressure increases with the wall expansion. At the same time the osmotic pressure of the cell sap decreases as a result of dilution. Finally the osmotic pressure reaches equilibrium with the wall pressure. The cell is then saturated and no more water can enter the cell. Under such circumstances the suction force is equal to zero.

II. A plant cell is placed in a very dilute cane sugar solution. Water flows into the cell and volume increases. But the flow stops before the saturation of the cell, when the osmotic pressure of the cell equals the sum of the wall pressure of the cell and the osmotic pressure of the solution surrounding the cell. This can be expressed by the following equation:

$$0 = W + o$$

where o indicates the osmotic pressure of the solution surrounding the cell. By substitution in equation I, we obtain $S = o$. In other words, when the volume of a cell remains constant in a solution of cane sugar, the osmotic pressure of the solution is equivalent to the suction force of the cell.

III. A plant cell is placed in a strongly hypertonic solution of cane sugar. Then the water flows out from the cell. The cell volume decreases and the wall pressure diminishes owing to contraction of the cell wall. When the cell reaches a state of incipient plasmolysis, the wall pressure is equal to zero. The wall is subject to no further contraction and the protoplasmic layer is detached from the cell wall. The apparent cell volume is subject to no further decrease.

Here we must make one point clear: that the out flow of water from a cell may also take place in a hypotonic cane sugar solution when the osmotic pressure of the solution is higher than the suction force of the cell.

2. Method of measuring the suction force of a plant cell

In 1916 Ursprung and Blum (11) suggested two methods. The first is by measuring the osmotic pressure of the cell sap and the wall pressure. The difference of these two will give suction force. This method involves too many measurements. At the same time great technical difficulties are involved.

The second method is comparatively simple. The principle underlying it is that when the volume of a cell remains constant in a solution of impermeable substance, the osmotic pressure of the solution is equivalent to the suction force of the cell. The details of the method are briefly outlined as follows:

The volume of the cell under investigation is first measured under paraffin oil. Then the paraffin oil is drained and the cell is transferred to a cane sugar solution of known concentration. After thirty minutes the cell volume is measured again to find out its volume change. Several neighboring cells of the same tissue are treated in the same manner but in solutions of different concentration. The volume change of different cells will show a gradation according to the concentration of the immersed solution. In this series, two concentrations will be found, in one of which the volume is slightly increased and in the other slightly decreased. By interpolation, the concentration in which the volume of the cell will remain constant is calculated. From the results of Berkeley, Hartley and Morse the osmotic pressure of the cane sugar solution is found. This method also involves many difficulties in technic, and rapid measurements are impossible. Moreover, this method gives only the measurement of a single cell.

3. Method of measuring the suction force of plant tissue

In 1923 Professor Ursprung and Blum (14) suggested another method which is still simpler. In this simple method plant tissue is measured instead of the individual cell. The plant tissue whose suction force is to be measured is immersed immediately in paraffin oil after it is detached

from the plant. Then strips of appropriate length are cut from the material under the paraffin oil. Length only is taken and thickness is entirely ignored in measurements. Since the length of the strip is generally thirty or forty times greater than the thickness, the variation in length can be used as a good index for the change in volume. The strip is first measured under the microscope in paraffin oil. The paraffin oil is drained and the strip is transferred to a cane sugar solution of known concentration, at a difference of .05 mol. From the change of the length of different strips the concentration at which the length of the strip remains constant can be interpolated. From the osmotic pressure table the suction force is determined.

4. The effect of external factors on suction force

In 1916 Professor Ursprung and Blum (9, 10) made a comparative study on the periodic fluctuation of the osmotic pressure of the plant cell sap and traced the effect of external factors on the osmotic pressure. From our previous discussion it is clear that any change in osmotic pressure in the cell sap will produce a corresponding change in its suction force. Experiments were also performed (8, 12) for the direct determination of the effect of external factors on suction force. However, the most comprehensive work was done by Blum (1, 5, 14) and Molz (3, 4).

Blum drew the following conclusion from his investigation, that all factors affecting the water relation of the plant will affect its suction force. Soil moisture is the most important of all. When the soil is dry the relative humidity of the air also exerts a great influence on suction force. Unfortunately Blum's original article is unavailable to the investigator, and he is not acquainted with the scope of the observation.

Molz obtained about the same conclusion as Blum, but put air humidity on the same rank of importance as soil moisture, especially in causing diurnal fluctuation in suction force. Temperature is said to be important in Winter. Other factors are considered to be of secondary, or of no importance. In studying the work of Molz, and of Prof. Ursprung and Blum, it appears that soil moisture has received adequate treatment, but there is room for further study about the effect of climatic factors.

II. OBJECT OF THIS INVESTIGATION

The subject of the present investigation is three-fold:

1. To study the effect of different climatic factors on suction force.
2. To study and ascertain the relative importance of different factors.
3. To obtain a large number of readings in order to apply statistical analysis.

III. SCOPE OF INVESTIGATION

The present investigation, as stated in the previous paragraph, is limited to the study of the effect of climatic factors on suction force. The work was carried on in Nankai University, Tien-tsin, China. The laboratory work covered two Summer months, July and August, 1927. The above stated period covered the rainy season of North China. At first it was intended to carry this work to the end of October, but on account of other duties it had to be discontinued in September.

In order to obtain a large number of comparable figures, the measurement was concentrated on the leaf of a particular species, *Syringa oblata*. Two neighboring bushes were chosen as experimental material so as to minimize the variation of

natural habitat. These two bushes are located on the middle of the south side of a tall building.

IV. METHOD AND PROCEDURE

1. Sampling of material for measurement: In sampling two points should be borne in mind. First, the sampling time must be so arranged that the measurements of the suction force of the leaf are well distributed in various climatic conditions. This will enable us to obtain a good distribution for statistical analysis, which is of primary importance in statistical study. In order to accomplish this, samples were taken at regular intervals throughout the day. The first sample was taken at 5 A.M. and additional samples were taken every two hours until 9 P.M. for the first four weeks and the last two weeks. During the middle two weeks, samples were taken hourly from 8 A.M. to 5 P.M. Before 8 A.M. and after 5 P.M. samples were taken at irregular intervals. The second important point in sampling is to take samples from leaves of approximately the same relative position. The position of leaves sometimes causes great variations in the environment of the leaves. For instance, the environment of a leaf under sunlight is entirely different from that of a leaf in shade. The factor that varies the most is sunlight intensity. Relative humidity also varies. For this reason, our sampling is limited to sun leaves. The environmental factors are by no means comparable in all sun leaves. The exposure and the angle towards the sun may cause great variation. For instance, a leaf standing parallel to the sun rays will not receive the same amount of light as a leaf lying horizontal. In sampling only those leaves lying horizontal or made to lie horizontal are taken.

From one leaf sometimes four to six samples are taken. Molz has shown that the influence of the evaporation of the cut surface extends only over a few millimeters. So in sampling the part about 5 millimeters from the cut edge is discarded.

2. Measurement of suction force: The sample is immediately put into paraffin oil after it is cut from the leaf. The suction force is measured with Ursprung and Blum's simplified method in the laboratory. The measurements are generally made from $\frac{1}{3}$ to 2 hours after sampling.

3. Watering: In order to determine specifically the effect of climatic factors, other disturbing factors must be brought under control. Of these, soil moisture is the most important and also is easy to control. The Syringa bushes are watered thoroughly once a day, about 8–9 A.M., so as to keep the soil moisture always in optimum condition.

4. Observations of climatic factors: Four factors are under observation. They are, air temperature, relative humidity of the air, sunlight intensity, and evaporation. The climatic factors, of course, include also wind and rainfall. But rainfall affects the water relation of the plants only indirectly through the enrichment of soil moisture. In our experiment, the soil moisture is always kept in optimum condition and rainfall will have no influence on the suction force except through its effect on relative humidity. This factor therefor is not included in our study. Wind exerts profound influence on the suction force of the leaf. But our experimental plants are located on the south side of a large building, and therefore are not exposed to strong wind action. Furthermore, during our experimental period there was wind on only two or three days; the readings, on this account, are not sufficient for our present study. This factor has also to be neglected.

Air temperature is recorded from the dry thermometer of a sling psychrometer

under shade. Relative humidity is taken with a sling psychrometer.

Sunlight intensity is measured by the difference of evaporation from a black and a white evaporating dish. The areas of the water surface of the two evaporating dishes are adjusted to be the same. The values are reduced to hourly gram basis.

Evaporation is measured by the hourly evaporation of the white evaporating dish. The location of the evaporating dishes is about the same as that of the Syringa plants. They are extended from a southern window of our laboratory.

The time of recording is also very important. In order to obtain good correlation the climatic factors should be recorded simultaneously with the measurements of the suction force. The climatic factors are recorded directly after the sample is taken. The whole process lasts about 10–15 minutes including the sampling.

V. RESULTS

The data compiled are too voluminous for this paper. The daily record is therefore reduced to weekly averages. The weekly average values or the suction force of the Syringa leaves and of the corresponding climatic factors for different hours of the day are tabulated in Table I.

In order to bring out the relation between the different climatic factors on the one side and the suction force on the other, the values from the above data are presented in graphic form in figure 1. The values of the suction force are plotted in pairs with each factor.

From the study of the before mentioned workers and from our own data, the suction force varies inversely with the relative humidity. Generally negative correlation can hardly be shown quantitatively on a graph. For this reason, the reciprocal of relative humidity is plotted

TABLE I

Daily fluctuation of suction force of Syringa leaf and climatic factors

DATE	HOUR	SUCTION FORCE IN ATM.	TEMPERATURE IN DEGREES C.	LIGHT INTENSITY IN G. H.	RELATIVE HUMIDITY IN PER CENT	EVAPORATION IN G. H.
July 13–16	5 A.M.	11.3	21.8		91	
	8	12.7	23.9		81	
	11	13.4	26.4		68	
	2 P.M.	14.5	27.4		67	
	5	13.5	26.6		75	
	8	13.1	24.9		84	
July 18–23	5 A.M.	10.8	23.7		91	.8
	8	12.6	28.0	1.2	79	1.7
	10	15.7	30.1	4.4	72	8.5
	12	15.6	30.7	4.6	68	10.8
	2 P.M.	16.3	30.9	5.6	68	12.9
	4	15.9	31.1	2.8	66	8.0
	6	13.5	30.3	1.8	72	5.1
	9	12.5	28.0		81	2.1
July 25–30	5 A.M.	11.2	24.0		89	1.7
	8	12.8	26.6	1.0	69	3.3
	10	16.0	30.6	4.7	62	11.7
	12	18.1	32.3	6.9	55	18.2
	2 P.M.	19.2	33.0	7.6	52	19.2
	4	18.0	32.3	5.0	56	14.7
	6	13.9	30.9	1.6	62	7.9
	9	13.3	27.9		78	4.1
August 1–6	5 A.M.	10.1	23.4		89	1.1
	8	13.9	27.0	1.6	74	3.2
	10	16.5	29.5	3.9	63	10.7
	12	17.6	31.0	6.3	56	17.4
	2 P.M.	18.2	31.6	7.0	52	19.5
	4	17.0	30.9	5.2	58	14.8
	6	14.0	29.0	1.9	65	8.1
	9	11.4	26.8		76	2.6
August 8–13	5 A.M.	11.2	24.1		88	1.9
	6:30	12.5	25.4		79	1.0
	8	14.6	27.9	2.1	71	3.4
	9	16.1	29.2	4.1	66	9.7
	10	17.3	31.0	5.1	60	13.4
	11	18.2	31.8	7.4	60	15.0
	12	18.0	32.6	6.2	53	14.8
	1 P.M.	18.1	33.1	6.7	52	16.7
	2	17.4	32.6	5.7	52	15.6

TABLE I—*Continued*

DATE	HOUR	SUCTION FORCE IN ATM.	TEMPERATURE IN DEGREES C.	LIGHT INTENSITY IN G. H.	RELATIVE HUMIDITY IN PER CENT	EVAPORATION IN G. H.
August	3	17.6	32.7	5.3	52	14.3
8–13	4	16.2	31.8	4.3	56	13.3
	5:30	13.7	30.6	1.8	61	7.2
	9	12.5	27.1		73	4.0
August	5 A.M.	11.2	20.9		92	1.3
15–20	6:30	11.8	21.9		86	0.7
	8	13.9	24.8	1.4	75	1.8
	9	14.8	25.8	2.0	71	5.9
	10	16.2	26.6	4.1	66	8.0
	11	16.5	27.8	5.2	61	10.6
	12	16.3	28.0	5.8	56	13.5
	1 P.M.	17.5	29.0	5.9	54	14.8
	2	17.1	29.3	5.8	52	15.0
	3	16.7	29.6	4.8	52	13.7
	4	15.8	28.7	4.3	56	12.2
	5:30	13.9	27.4	1.8	60	8.0
	9	13.1	24.4		73	2.9
August	5 A.M.	10.7	20.8		90	
22–27	8	11.7	22.8	1.3	87	1.8
	10	12.9	24.3	2.3	80	6.1
	12	14.8	26.1	4.5	77	8.5
	2 P.M.	15.9	26.8	5.7	73	13.7
	4	14.4	26.5	4.1	73	12.0
	6	14.0	25.3	1.0	75	5.8
August 29–	6 A.M.	12.2	23.2		85	
September 3	8	12.6	24.2	1.5	82	2.9
	10	14.7	26.2	3.1	70	8.5
	12	16.0	27.0	3.3	70	10.2
	2 P.M.	17.1	28.2	4.0	68	13.7
	4	15.4	27.5	3.5	70	10.6
	6	13.2	26.7	.5	75	6.6

instead. By this means, the correlation is converted from negative to positive, and the trend of the two curves can be easily compared.

The graphs present in clear manner the following simple facts. First, the suction force of the Syringa leaf shows a rhythmical diurnal fluctuation. Secondly, this diurnal fluctuation is brought about by the fluctuation of the various climatic factors. Thirdly, all factors seem to exert profound influence on the suction force. The first two findings agree entirely with the results of the previously mentioned workers. The third, however, is not in perfect agreement with their results, especially with regard to light and temperature. We shall analyse the effect of each individual factor separately in the following paragraphs.

TABLE II

Suction force and temperature

SUCTION FORCE IN ATM.	AVERAGE AIR TEMPERATURE IN DEGREES C.	NUMBER OF MEASUREMENTS
8.1–9	21.3	6
9.1–10	22.8	10
10.1–11	24.1	15
11.1–12	24.8	35
12.1–13	24.9	52
13.1–14	27.2	46
14.1–15	28.0	56
15.1–16	29.2	52
16.1–17	29.2	31
17.1–18	29.8	31
18.1–19	30.9	13
19.1–20	31.7	18
20.1–21	33.6	14
21.1–22	33.0	5
22.1–23	33.7	3
23.1–24	37.0	1

1. Temperature and suction force

According to Molz air temperature exerts very little influence on the suction force in Summer. But from our data, the correlation seems quite high. The results are tabulated in Table II.

From the complete data, the correlation coefficient is calculated according to Pearson's formula. The value obtained is .678. From the statistical point of view any correlation higher than .6 indicates good correlation. In other words, air temperature does exert influence on the suction force of the leaf. Here we must

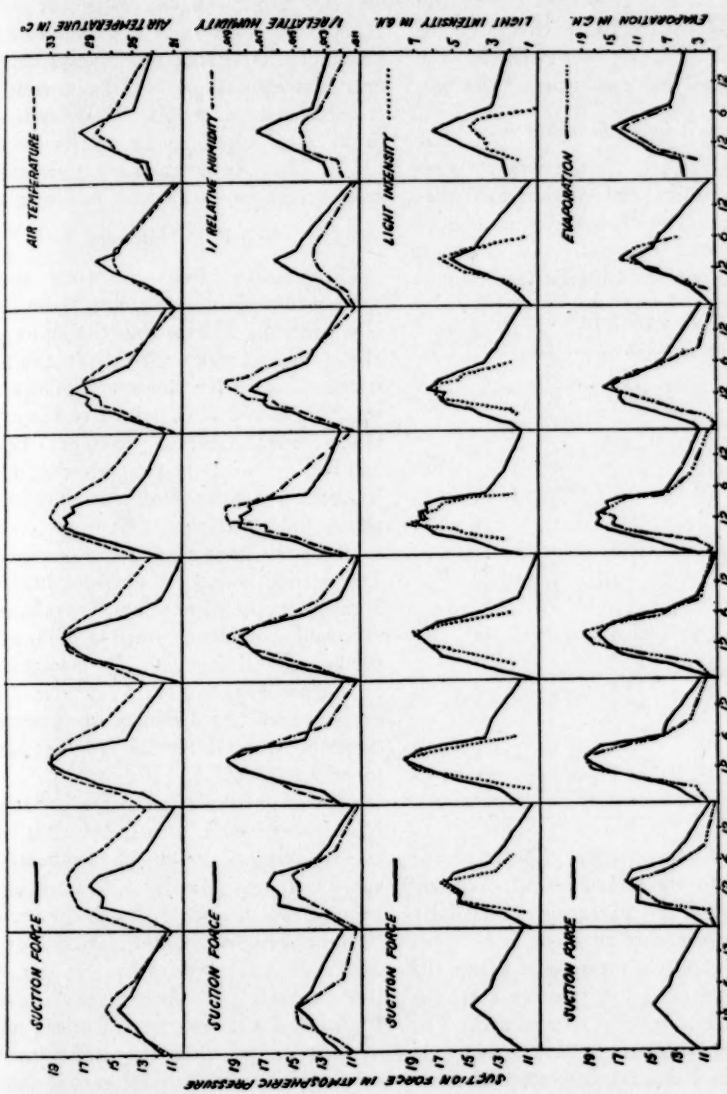

FIG. 1. DAILY FLUCTUATION OF THE SUCTION FORCE AND CLIMATIC FACTORS

not overlook the fact that other climatic factors are operating simultaneously on the suction force. This high correlation may be partially due to the effect of some other factors. This point will be discussed in detail in one of the later sections.

2. *Relative humidity*

That high correlation exists between relative humidity and suction force has been recognized by Blum and Molz. Both of them considered relative humidity as the most important climatic factor in its influence on suction force. The results of the present investigation partially confirm their work. The correlation is especially high when the suction force is between 8.1–22 atmospheric pressures. When the suction force is higher than 22 atm. the correlation is not very pronounced. The data of the present investigation are presented in Table III in condensed form.

TABLE III

Suction force and relative humidity

SUCTION FORCE IN ATM.	AVERAGE RELATIVE HUMIDITY IN PER CENT	NUMBER OF MEASUREMENTS
8.1–9	92.2	6
9.1–10	89.5	10
10.1–11	87.7	15
11.1–12	82.1	35
12.1–13	81.5	52
13.1–14	72.7	46
14.1–15	69.1	56
15.1–16	64.0	52
16.1–17	60.9	31
17.1–18	58.2	31
18.1–19	50.3	13
19.1–20	48.7	18
20.1–21	49.8	14
21.1–22	45.0	5
22.1–23	46.3	3
23.1–24	53.0	1

The calculated correlation coefficient is $-.777$. It is much higher than that of the temperature. In other words relative humidity exerts greater influence on suction force than air temperature. Blum maintains that relative humidity of the air becomes important only when the soil is dry. During the present experiment the soil moisture content was always kept at optimum condition, yet the correlation coefficient of the relative humidity is very high. Our experimental results indicate that Blum seems to have overemphasized the importance of soil moisture.

3. *Light intensity*

Theoretically light intensity should exert profound influence on suction force. It is generally known that the major part of the sun's energy which the leaf receives is consumed in transpiration. The transpiration of the leaf is greatly increased, when the leaf is exposed to light. Brown and Escomb's classical experiment, which has been quoted in most plant physiology texts, indicated that 48.39 per cent of sunlight is consumed in transpiration. The author finds that two cut leaves of Syringa exposed horizontally to the sun's rays will transpire as much as eight grams per hour, while in shade, its transpiration seldom amounts to a gram per hour. This excessive amount of transpiration certainly exerts a strong influence on the suction force of the leaf.

Molz, however, basing on a few laboratory experiments, concluded that light exerts very little or no influence on suction force. Hayoz (3) found an increase in suction force due to the presence of light in two of the three series of experiments which he performed; in the third one he failed to observe any increase. By careful examination of the data, it appears to me that the light intensity employed by these investigators may not be strong enough in comparison with sunlight. In Hayoz's experiment the light intensity reaching the experimental material is only sufficient to heat a black

bulb thermometer to 35 degrees C. The black bulb thermometer installed in a box exposed to the sunlight in Tientsin was generally heated to 80–90 degrees C. during noon time. On a few days the temperature recorded by the black bulb thermometer was over 90 degrees C. In Hayoz's experimental condition, the increase recorded as 1.7 atm. It is self-evident, then, that much stronger intensity in sunlight will bring greater increase.

Now let us examine the results of the first series of experiments conducted by Molz. He first exposed the experimental plant material to a radiant energy of 0.000004 cal. cm²/sec. and obtained an increase of 3 atm.; secondly to a radiant energy of 0.000011 cal. cm²/sec. and obtained an increase of .8 atm.; thirdly to a radiant energy of 0.0001 cal. cm²/sec., and obtained an increase of .6 atm. In the first two experiments the results seem to indicate a tendency to proportional increase of suction force with increase of the amount of radiant energy received. But the result of the third experiment fails to indicate that tendency. In comparing the first and the second, the increase in radiant energy is about 2.7 times and the increase in suction force is also 2.7 times. But in comparing the first and the third the increase in radiant energy is 25 times, while the increase in suction force is only two times. But we must understand that we are dealing with a living organ of a plant, the individual variability of which is a great disturbing factor in such relation. We certainly can not expect to find a mathematical relation from three readings. Moreover, unavoidable error in measurements may also introduce a considerable amount of error into such kind of data, since the increase is so small. A difference of .01 mol. in concentration will introduce an error of from .3 to .4 atm. Any investigator acquainted with the present method will realize that error of such magnitude is unavoidable. So non-conformity of results from three experiments is not a surprising fact. At the same time we must realize that an increase of .6 atm. under an exposure of radiant energy of .0001 cal. cm²/sec. is considerable, when we think that the maximum radiant energy of the sunlight received by a horizontal surface in July and August, according to Kimball (7), is 1.5–1.7 cal. cm²/min. It is equivalent to .025–.028 cal. cm²/ sec. or is 250–280 times greater than the radiant energy used in Molz's experiment.

TABLE IV

Suction force and light

SUCTION FORCE IN ATM.	AVERAGE LIGHT INTENSITY IN G. H.	NUMBER OF MEASUREMENTS
9.1–10	0.5	1
10.1–11	1.5	2
11.1–12	1.2	9
12.1–13	1.3	19
13.1–14	2.1	33
14.1–15	3.0	44
15.1–16	4.8	48
16.1–17	4.3	27
17.1–18	5.7	28
18.1–19	5.8	13
19.1–20	6.4	18
20.1–21	7.1	14
21.1–22	7.9	5
22.1–23	8.0	2
23.1–24	6.5	1

In the second series of experiments Molz failed to obtain any possible results showing increase of suction force due to exposure to light. In these experiments he exposed the upper half of the leaf of maize to light or other form of radiant energy and kept the lower half of the leaf in darkness by means of a screen. The exposure varied from 2–16 hours. At the end of the experiment the difference in

suction force between the lighted half and the screened half was not determinable. Two explanations can be offered for this fact. The first is that light exerts no influence on suction force. The second is that the suction force of the whole leaf is interrelated. When one part of the leaf is affected, the influence may extend over the whole leaf. Molz apparently was inclined to accept the first explanation, but the author feels that the second interpretation is more plausible, especially with reference to the maize leaf. The leaf of maize is parallel veined. The mesophyll cells bordering the vascular elements in both the upper and the lower half absorb their water from the same source, viz. the water column in the vascular elements. When the suction force of the cells in the upper half of the leaf is raised, the tension of the water column in the vascular elements will increase correspondingly. The increased tension will render absorption by cells in the lower part of the leaf more difficult. The difficulty in absorption in turn will cause a corresponding increase in suction force. Thus an increase of suction force in the upper half due to exposure to light will produce a corresponding increase of suction force in the lower screened half of the leaf. We may therefore feel safe in saying that the result of Molz's second series of experiments is not a conclusive proof of the ineffectiveness of light on suction force.

Our results based on a large number of observations, which amounts to 264, indicated a distinct correlation between the light intensity and the suction force. The results are tabulated in Table IV.

The correlation coefficient of light intensity and suction force is found to be .7, which lies between that of air temperature and that of relative humidity. In other words, the effect of light intensity on suction force is greater than the effect of temperature and less than that of relative humidity.

4. *Evaporation*

To the author's limited knowledge, the correlation of evaporation and suction force has not been previously studied. Theoretically these two should give a very high correlation coefficient, because the evaporation and the suction force are subject to the influence of the same set of climatic factors. Evaporation represents the summation of the effect of all climatic factors, i.e., air temperature, relative humidity of the air, sunlight intensity, wind, etc. The results of the present investigation, which confirm our speculation, are tabulated in Table V.

TABLE V

Suction force and evaporation

SUCTION FORCE IN ATM.	AVERAGE EVAPORATION IN G. H.	NUMBER OF MEASUREMENTS
8.1–9	1.4	5
9.1–10	2.5	4
10.1–11	2.8	9
11.1–12	2.5	26
12.1–13	3.9	34
13.1–14	7.6	39
14.1–15	11.1	49
15.1–16	17.0	48
16.1–17	16.2	29
17.1–18	20.0	28
18.1–19	21.1	13
19.1–20	23.5	18
20.1–21	25.0	14
21.1–22	29.0	5
22.1–23	30.0	2
23.1–24	25.0	1

The preceding table indicates that the corresponding two factors show very high correlation. The calculated correlation coefficient is .828. Such exceptionally high correlation is within our reasonable expectation. It is interesting to note that the multiple correlation coefficient of the three direct climatic factors is .812,

which is still a little less than that of evaporation. This is due to the fact that evaporation represents the effect of all climatic factors; while the latter represents only the effect of three important factors. On account of this exceptionally high correlation coefficient the value of evaporation per hour may be used as the index for the suction force of the leaf with distinct advantage.

5. The total effect of all climatic factors

Among all climatic factors, light intensity, air temperature, and relative humidity are constantly operating factors. Other factors are intermittent. For instance, wind came on only two or three days during the whole period of investigation. By the total effect of all climatic factors we mean the total effect of all constantly operating factors. This is known as multiple correlation in statistics. The multiple correlation coefficient is calculated according to Kelly's formula (12). Before calculation, the measurements made when there is no light are parceled out. The calculated multiple correlation coefficient is .812. This indicates exceptionally high correlation. In other words, when the soil moisture is kept in optimum condition, the climatic factors are the determinant factors causing the fluctuation of the suction force.

6. The actual effect of the individual factors and their relative importance

The correlation coefficients for each climatic factor found in the previous paragraphs are as follows:

Relative humidity	−.777
Air temperature	.678
Light intensity	.700

However, these figures are not good criteria for comparison, since they represent, not the true effect of those particular factors, but their effect with additional influence from other factors. In order to obtain the true correlation of each individual factor, other disturbing factors should be kept constant. Of course, such a condition can be created only in the laboratory. When a large number of measurements is desired, the work is exceedingly laborious.

However, we may use a mathematical tool, what is known as partial correlation in statistics. By the method of partial correlation, we can isolate the effect of any of the variables. Yule's formula (15) is used for calculation. Before calculation we have to isolate those measurements, which are taken when all constant climatic factors are operating. This means that the measurements taken during the evening and in the early morning are not included in the calculation. The calculated partial correlation coefficients for various climatic factors are tabulated in the following table.

Air temperature	.163
Light intensity	.445
Relative humidity	−.469

From the preceding table it is clear that the influence of the air temperature is very slight. This finding agrees with that of Molz, that air temperature plays a minor rôle in modifying the suction force during the Summer months. It also indicates that relative humidity is the most important; this again agrees with Molz's finding. But in one respect, our results differ from his. According to him the effect of light intensity is of little or no importance as stated before. Our experiment shows very clearly that light exerts a great deal of influence on suction force. The partial correlation coefficient of light intensity, which represents the isolated effect of light on suction force, is as high as .445. Its influence is only a little less than that

of relative humidity, whose partial correlation coefficient is −.469.

7. *Variation of relative importance of different climatic factors during different hours of the day*

Now let us examine closely the graphs in figure 1, which represent the weekly average value of the suction force and of various climatic factors. The trend of those graphs seems to indicate that the influence exerted by different climatic factors on the suction force varies with the hours of the day. In order to clarify this point, the measurements taken at different hours of the day are separated into four groups. The first group includes the measurements taken from 6:30 A.M. to 10 A.M.; the second group, from 10 A.M. to 2 P.M.; the third group, from 2 P.M. to 6 P.M.; and the fourth group, from 6 P.M. to 6:30 A.M. of the next day. For each group the partial correlation coefficients of different climatic factors are calculated and tabulated in Table VI.

TABLE VI

Partial correlation coefficient of suction force and climatic factors in different periods of the day

HOURS OF THE DAY	PARTIAL CORRELATION COEFFICIENT		
	Air temperature	Light intensity	Relative humidity
6:30 A.M.–10 A.M.	.195	.345	−.464
10 –2 P.M.	.211	.151	−.564
2 P.M. –6 P.M.	.198	.526	−.253
6 –6:30 A.M.	.229		−.250

From the preceding table we can obtain the following conclusions. In the first place the relative importance of different factors varies with the hours of the day. From 6:30 A.M. to 10 A.M., both relative humidity and light intensity are controlling factors, but relative humidity is slightly more important. From 10 A.M. to 2 P.M. light intensity plays a very insignificant rôle in affecting suction force. Its influence is even less than that of air temperature. During that period relative humidity of the air is the most important factor. From 2 P.M. to 6 P.M. the reverse is true, relative humidity of the air ceases to be important and light intensity becomes the key factor. After 6 P.M. light ceases to exert its influence. The influence of relative humidity remains very low; it is about equal to that of air temperature. Their partial correlation coefficients are only a little above .2, which is considered to be rather insignificant. In other words, the climatic factors exert only a slight influence on suction force in the night time. This is probably due to two causes. In the first place stomata close at night. Secondly the cell sap concentration may undergo internal adjustment due to enzymic reaction (6).

On the whole the influence of air temperature on the suction force is comparatively insignificant and varies within a very narrow range throughout the whole day.

VI. SUMMARY

1. The object of this investigation is to study the effect of climatic factors on the suction force of the leaf of *Syringa oblata*, when the soil moisture is kept in optimum condition. The investigation was performed in July and August, 1927.

2. Among the climatic factors, air temperature, light, and relative humidity are recorded simultaneously with the measurements of the suction force, and rainfall and wind are neglected. The former is neglected because it exerts its influence only indirectly through enrichment of soil moisture, which has been kept constant in the present investigation.

The second is omitted because it is present only on rare occasions.

3. Evaporation is measured simultaneously with other climatic factors, because it represents the combined effect of all climatic factors.

4. In sampling only the leaves which lie horizontal or are made to lie horizontal are taken in order to eliminate the influence of exposure.

5. A large number of measurements were taken in order to be able to use statistical methods to analyse the data. The total number of measurements taken amounts to 388.

6. The suction force of the Syringa leaf shows a rhythmical diurnal fluctuation which is caused by the fluctuation of climatic factors.

7. Our results confirm, in one respect, the results of Blum and Molz, i.e., that the relative humidity is the most influential factor on suction force. Its partial correlation coefficient is $-.469$.

8. Our results disagree with Molz in regard to the effect of light. We find that light exerts a very profound influence on suction force. Its influence is only a little less than that of relative humidity. Its partial correlation coefficient is .445.

9. Our results are in accordance with that of Molz in regard to the effect of temperature. Its influence on suction force is comparatively insignificant. Its partial correlation coefficient is .165.

10. The total effect of air temperature, light intensity, and relative humidity on suction force of the leaf is represented by a large multiple correlation coefficient which amounts to .812.

11. The correlation coefficient of evaporation and the suction force is .828. It is even higher than the total effect of temperature, light, and relative humidity, because it represents the total effect of all climatic factors, including both constant and intermittent factors.

12. The relative importance of different climatic factors varies with the hours of the day. From 6:30–10 A.M., both light and relative humidity exert strong influence but the latter in a slightly higher degree. From 10 A.M.–2 P.M., relative humidity is the key factor while the influence of light intensity is even less than that of temperature. From 2–6 P.M., light intensity is the key factor, the influence of relative humidity is comparatively insignificant. From 6 P.M.–6:30 A.M., the effect of climatic factors on suction force is much less in degree. The partial correlation coefficients of both air temperature and relative humidity are about .2. Temperature remains an insignificant factor throughout the whole day.

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NEW BIOLOGICAL BOOKS

The aim of this department is to give the reader brief indications of the character, the content, and the value of new books in the various fields of biology. In addition there will frequently appear one longer critical review of a book of special significance. Authors and publishers of biological books should bear in mind that THE QUARTERLY REVIEW OF BIOLOGY *can notice in this department only such books as come to the office of the editor. The absence of a book, therefore, from the following and subsequent lists only means that we have not received it. All material for notice in this department should be addressed to Dr. Raymond Pearl, Editor of* THE QUARTERLY REVIEW OF BIOLOGY, *1901 East Madison Street, Baltimore, Maryland, U. S. A.*

THE MECHANICS OF TELEOLOGY

Being a review of *Blood. A Study in General Physiology*, by Lawrence J. Henderson. New Haven (Yale University Press) 1928. 5¾ x 9; xix + 389. $5.00.

By Joseph Berkson, Institute for Biological Research, Johns Hopkins University

The science of biology, says Henderson, is the record of efforts accurately to describe and clearly to understand living things. The definition wears plausibility and conviction on its face, but a realistic examination of the activities of most operating biological scientists would render it exceedingly dubious. Of descriptive data there is a vast and ever growing output, but contributions to the synthesis of observations under simple and general concepts, which is, broadly, the way by which scientific understanding is achieved, are rare. Far from being acutely conscious that comprehension is the essential part of their professional task, biologists have come to suspect a work characterized by any degree of thoughtfulness; "philosophical" and "metaphysical" applied to scientific endeavor are actually used as terms of opprobrium. Such a condition could not obtain in a community of genuine thinkers, but it is no discovery of ours that scientists are not often thinkers.

The book under review, the author's Silliman Lectures for 1928, somewhat amplified, fulfils to an eminent degree the obligation implied by his own definition of biology. Observations, many of them of great technical refinement, are abundantly presented, but more significantly they are subsumed under an idea which is a distinct and important contribution to the comprehensive understanding of biologic phenomena. Appropriately enough in the light of what we have remarked in our opening paragraph, it has been subjected to an impassioned attack, on the grounds of its metaphysical character, by one of the leading contributors in the very field of investigation covered by the book. Countering this, other equally distinguished scientists have spoken loving and soothing words about it. The series of appreciative comments is to be found in *Science* in the numbers of January 11 and February 8, 1929, and may be recommended for its entertainment as well as instruction.

And now for the book itself, first the factual matter. It deals with the red blood of vertebrates studied as a "physicochemical system and as a tissue." Delimited so, and neglecting an emphasis on multiple factors unique in this author and

to be discussed later, it brings together investigations on the blood that have been in progress now for many years. The elucidation of the physiologic rôles played by the ions of sodium, potassium, carbonates, phosphates and chlorides, as well as the chemical character and biologic function of hemoglobin and other blood proteins, the study of equilibrium among these out of and in the body, the solution properties of CO_2 and O_2 in the blood, all form a necessary part of the basis for the work. Names recalled prominently but not exclusively in this connection are Barcroft, Bohr, J. Haldane, Y. Henderson, Krogh, Michaelis, Van Slyke, Warburg, as well as L. J. Henderson. The work in hand comprehends these, not in the character of a compendium of their results, but rather rests on them for a synthesis that is itself novel and creative.

Blood as a physico-chemical system may be considered as made up, to a first degree of approximation, of water, certain bases, hydrochloric, carbonic and other acids, proteins and oxygen. These are disposed among two phases, plasma and cells, in eight components: "(1) Water, H_2O. (2) Carbon dioxide, CO_2. (3) Oxygen, O_2. (4) Hydrochloric acid, HCl. (4a) The sum of all other acids except proteins (that is, excluding carbonic and hydrochloric acids and proteins) which are combined with base, HX. (5) The sum of all the bases (except protein) of the plasma (or serum), BOH_s. (6) The sum of all the bases (except protein) of the cells, BOH_c. (7) The sum of the proteins of plasma (or serum), P_s. (8) The protein of the cells, P_c or, approximately, Hb." The constitution of these under usual normal conditions is constant except for alteration incident to the exchange of CO_2 and O_2 in the lungs and tissues. What happens in the blood when the exchange takes place?

When carbon dioxide enters or leaves the blood there is a disturbance of equilibrium in both plasma and cells between this substance, the bases, and the other weak acids. If for convenience we neglect the phosphates and other similar compounds included in the component HX and also the ionization of hemoglobin as a base, we may represent the process by the two reversible reactions:

$$H_2CO_3 + BP_s = BHCO_3 + HP_s,$$
$$H_2CO_3 + BP_c = BHCO_3 + HP_c,$$

and we may say that the absorption of carbonic acid in varying amounts by blood is chiefly due to the transfer of base from proteins to carbonic acid. It must be noted that the above reactions are greatly simplified schemeta, for the proteins are far from being simple monobasic acids.

When the entrance of carbonic acid into the blood, accompanied by these two reactions, takes place, there must evidently be an increase in the concentration of free carbonic acid, of bicarbonate, and of those protein molecules in which certain acid radicals are free, and a decrease of the concentration of protein molecules in which certain acid radicals are ionized as salts. Hence there result two further changes in the system: (1) An increase in the hydrogen ion concentration, and (2) an increase in the total concentration of dissolved substances.

In general these changes of concentration, resulting from the addition of a small quantity of carbonic acid to the system, will be of different magnitudes in cells and in plasma. . . . . A condition of equilibrium in respect of hydrogen ions and of water existed before the addition of carbonic acid, but as a result of the changes following the addition of carbon dioxide unequal changes in the concentrations of these substances must have taken place in cells and in plasma, since increase in bicarbonate is accompanied, under these circumstances, by diminution of hydrogen ion concentration and by increase of osmotic pressure. Thus there must exist a tendency for acid and for water to pass from plasma to cells in order to re-establish the disturbed heterogeneous acid-base equilibrium and the disturbed osmotic equilibrium. In accordance with these considerations, the addition of carbonic acid to blood is, in fact, followed by a movement of water and of hydrochloric acid and other acids into the cells from the plasma.

We see then, that not one thing happens, but many, and in addition each effect becomes a link in a concatenation of events that modifies and is modified by all the rest. This is a simplified statement of

only part of the facts and does not touch the changes incident to the entrance of oxygen into the blood, but even so the mind is bewildered in any attempt to grasp them in detail and their totality. Moreover scientifically it suffers from the fatal weakness of not being quantitative. How then to retain the complexity of the whole and at the same time submit it to quantitative treatment is the problem at hand. The mathematical method of equational statement is suggested. Granted that the necessary relations between the physiological variables CO_2 and O_2 and all the other pertinent descriptive variables of the blood, such as pH, cell volume, combined hemoglobin, etc., be known quantitatively, we may express each of the variables separately as a mathematical function of CO_2 and O_2, in an equation. The resulting series of equations, taken together, constitutes a sufficient description of the facts relevant to the equilibrium among the components. For if now the condition of CO_2 and O_2 be known, the condition of any variable is given by one of the equations, and always quantitatively as a certain number of appropriate units. Or, again, if instead of CO_2 and O_2 the condition of two other variables be known (two will always be necessary in the situation under discussion) one may likewise obtain the condition of any third by the simultaneous solution of appropriate equations in the series. Though quite adequate, this equational method of comprehending the facts quantitatively is not the only thinkable one, and Henderson prefers to use another, the nomographic. Since Descartes gave us analytical geometry, it has been possible to represent algebraic relations geometrically, and in an elementary form the nomographic method consists of representing two variables on Cartesian coördinates, and a third as contour lines running across them. If this procedure is followed for all the equations in a complete series representing the equilibrium conditions among the components of the blood we have again, as before, a sufficient description of all the pertinent facts for that sample of blood. The resulting nomograms are necessarily numerous, or if superimposed exceedingly complex and the whole cumbersome. For these reasons the author discards this method for the technique adopted as final, the alignment chart of D'Ocagne. In this, each of the variables descriptive of some condition of the blood, is represented on a line more or less vertically disposed on a chart, and on it are scaled off all the possible values which that variable can assume. The values of any two conditions being given, they are located on the appropriate scales and a straight line drawn through them; the line will of course cross all the other scales and the intersecting points represent the simultaneous values of all the variables. Here we have graphically presented a point already made. On this form of representation a straight line stands for the total constitution of a sample of blood. Since two points determine a line, it becomes strikingly evident that a definite condition of any two variables fixes at once the condition of all the rest. Shifting conditions of the blood traced through the evaluation of two variables may be followed in their totality by way of the shifting position of their correlated lines on the nomogram. Henderson utilizes the nomographic method thus to study the changes occurring in the blood during the respiratory cycle, in rest and work, in health and disease, and in different species. We shall not follow him here, for we wish to conserve the space available to us for the consideration of aspects of his work which are of broader interest.

We have elaborated in considerable de-

tail and at some length the nomographic methodology of the author, as he himself has also done, because it is essential to the presentation of the ideas advanced by him. The concept of the blood as a multiple unity rather than the sum of a number of individual constituent elements is well conveyed in the nomographic representation, and is replete with implication for the objectives to be sought in the scientific investigation of its physiological activity. The unity is conceived as a state of heterogeneous equilibrium expressed as a mathematical function, and here Henderson is influenced importantly by the writings of Willard Gibbs and Vilfredo Pareto. As illustrating the point, in connection with a particular problem, we may quote the search for what it is, in the blood acting on the respiratory center which stimulates breathing. The attempt to allocate it in the pH or CO_2 or some other factor is, if we adopt the view of Henderson as a thorough-going guide, wrongly conceived, an example of what Whitehead has referred to as the "fallacy of misplaced concreteness." Since no single component of the blood changes without a simultaneous alteration of the rest, may it not be that the stimulus of respiration in the circulation is no substance but a certain range in the equilibrium conditions?

A sample of normal blood is a line on the nomogram and the intersections on the scales the necessary concomitant values of the descriptive variables. *The relationship among these is not casual.* Minute examination of them reveals the general truth that they are such as to preserve a constancy in those conditions which make for efficiency in the economy of the organism. "Stability of hydrogen ion concentration is a property of all forms of blood and also of the waters of the earth. In higher organisms this condition is, however, insured by elaborate physiological regulatory processes. Constancy of osmotic pressure of blood is less general, but seems to have been acquired at a relatively early stage of evolution. Constancy of temperature insured by physiological regulation is peculiar to the birds and mammals. It seems probable that temperature and osmotic pressure in the higher vertebrates are approximately optimal conditions for the activities of protoplasm. In the case of the hydrogen ion concentration there can be no doubt that this is so." Henderson makes much of the point, and sees in it a remarkable corroboration of the idea of a constancy in the *milieu intérieur* enunciated by Claude Bernard. "In his opinion (Bernard's), which I can see no reason to dispute, the existence and the constancy of the physico-chemical properties of these fluids is a necessary condition for the evolution of free and independent life. This theory of the constancy of the *milieu intérieur* was an induction from relatively few facts, but the discoveries of the last fifty years and the introduction of physico-chemical methods into physiology have proved that it is well founded." At this point we may give our attention to an objection expressed by J. Haldane against this view of Henderson's (*Science*, April 26, 1929). The physico-chemical system of the blood is not to be considered a physiological *milieu*, he argues, but merely physico-chemical, and it is not an aspect of physiology proper at all. The regulation of constancy which *is* physiological is accomplished by the lungs and kidneys. "In actual fact this constancy depends during health on the coördinated activity of the kidneys and respiratory organs, in accordance with Bernard's principle. . . . . Not all the buffering in the world would keep the reaction constant otherwise, though the buffering greatly smooths the regulation." (*Science*, *ibid.*). The objection of Haldane, it seems to us,

is not well taken, and when met serves to illustrate the depth of insight which characterizes Henderson's view. The latter has long insisted on the reciprocal character of adaptation (*The Fitness of the Environment*. New York (The Macmillan Co.), 1913) and following him we may say that no amount of activity on the part of the kidneys and lungs would necessarily secure constancy of reaction, were not the blood so constituted as to be adjusted to these activities. How and why should an objective science differentiate between the parts of such a functioning unity? The physico-chemical constitution of the blood by which its parts are integrated in just such a way as to insure physiological efficiency is not irrelevant to physiology, but as Henderson insists, central to it.

Our comments have deliberately related the contents of the book to the specific business of elucidating the physiological activities of the blood. We would not otherwise faithfully reflect the thoroughgoing experimental character of its major portion. In the opening and closing chapters, however, and interspersed between is contained a contribution toward a philosophy of biologic science which forms in itself a notable document in the history of scientific thought. Henderson has been a watchful observer of the varying modes in the attitude of reason to the nature of the physical world and he knows what it is all about.

> Like all our enterprises the sciences are changeable. They grow and develop. At first descriptive and classificatory, then rational, in this twentieth century some will say that they are destined to become metaphysical. But before they can attain to this last condition it seems probable that they must pass through a stage in which all is clarity, simplicity, and order, where there is no room for philosophic doubt and where, by a singular paradox, the adoption of approximations and philosophically dubious abstractions yields certainty, or at least the closest approach to certainty that man has ever known.

The sly wisdom exhibited in this statement precludes the offering of nicely complete solutions by its author. Aware keenly of the inadequacy of purely mechanistic conceptions for the investigation of biologic problems, but equally conscious of the tremendous value they have had for the progress of science, and at the same time recognizing the intellectual sterility of vitalism, he has in his *Fitness of the Environment* and *Order of Nature* done much to give the dilemmas clarifying analysis. In teleology he sees a concept promising but vague, and has struggled to trace for it a more definite connotation. In assimilating it to mathematical statement and the notions of heterogeneous equilibrium of Willard Gibbs, while offering at the same time for its handling the nomographic technique, he has, it seems to us, made definitive progress in giving it a formulation available for the scientific laboratory. Some of the other expressed thoughts, particularly those associated with the idea of defining life in terms of improbability, appear to us pregnant with the possibility of similar usefulness, and merit a diligent effort at elaboration.

We should not close without the comment that the whole bears relation to the attempt now current among those aristocrats in the world of thought, the speculative philosophers and theoretical physicists, to develop an organic philosophy of nature. Coming from a proletarian of the biological laboratory and couched largely in terms of his own experimental results, it has an exceptional meaningfulness.

BRIEF NOTICES

EVOLUTION

PALAEONTOLOGY AND THE EVOLUTION OF MAN.
By D. M. S. Watson. Oxford University Press
70 cents $5\frac{3}{4}$ x 9; 27 (paper) *New York*

This is the Romanes lecture of 1928. It is an interesting review of what a conservative paleontologist is able to say at the moment regarding man's evolution. The general conclusion is that "man has indeed arisen from an ancestral ape, differing from the modern forms in his less intense brachiating specializations. Man has undergone his own evolution since that period, and the changes which have occurred in his structure are related to habits entirely different to those of the apes."

GENETICS

VOYAGES OF EXPLORATION TO JUDGE OF THE BEARING OF HYBRIDIZATION UPON EVOLUTION. I. *South-Africa. Genetica Vol. X.*
By J. P. Lotsy and W. A. Goddijn.
Martinus Nijhoff
35 guilders for 2 vols. *The Hague*
Vol. I, $6\frac{1}{2}$ x $9\frac{3}{4}$; viii + 315
Vol. II, $7\frac{1}{4}$ x 10; 11 plates

An analysis of biological variation is still the root problem of evolution, as it was when Darwin wrote. Since his time we have come to appreciate, notably through the work of Johannsen, that not all types of diversity seen in nature are of equal significance for the evolutionary process. The senior author of this book has set himself the task of estimating how large a share of the diversity that exists is due to hybridization. Towards this end he explored many parts of the world where observations bearing on the question are available. This report, treating of South Africa, is the first of a number to be issued. With the junior author he observed the results of hybridization in the flora and in man and his general conclusion, given explicitly only for man, is that

> hybrids between different human races and their segregates showed . . . . the great diversity arising from hybridization. Nobody, who looks at the matter in an unprejudiced way, can possibly believe that the different races of mankind in S. Africa or elsewhere have arisen by mutation. A Bushman mutates as little so as to form a Bantu, as a European does or the reverse.

The treatment is descriptive throughout, the examples abundant and detailed. There are a large number of illustrations including a set of beautiful colored plates supplied in a separate packet, and an index, but no bibliography.

SCIENTIFIC PAPERS OF WILLIAM BATESON. *Volumes I and II.*
Edited by R. C. Punnett. The Macmillan Co.
$28.50 per set *New York*
Vol. I, 7 x 10; viii + 452
Vol. II, viii + 503

These two volumes contain, with a few exceptions, all of Bateson's purely scientific papers. The first volume includes his papers on variation, the second those on heredity. Bateson is one of the great figures of modern biology, and his papers are of first rate importance to any student of the history of science. There is an index in each volume and a bibliography in Volume II. In appearance they are up to the high standard of the Cambridge University Press.

REVISED ENCYCLOPEDIA OF CAGED BIRDS. *Canaries, Parrakeets, Finches, Mules and Hybrids. Advice, Suggestions and Information for Pleasure and Profit.*
By Howard Fogg and Nola Miller Fogg. *Audubon Publishing Co.*
$1.50 (cloth) 6¾ x 10; 144 *Louisville, Ky.*
.75 (paper)

A revised and enlarged edition in bird culture in which the author, who is managing editor of the *Canary Journal and Bird World*, has brought together in handy form much information concerning the selection and breeding of cage birds; their treatment and feeding when ill as well as in good health; bird diseases; hints on building breeding cages; descriptions of the various breeds; training of the roller canary, etc. There are numerous illustrations, including a number of group pictures of bird fanciers, which have apparently been thrown in for good measure, and an index.

MATERIALS FOR THE STUDY OF INHERITANCE IN MAN.
By Franz Boas. *Columbia University Press*
$10.00 6 x 9; viii + 540 *New York*

In this volume Prof. Boas puts at the disposal of human biologists all of the original data upon which was based his famous study on *Changes in the Bodily Form of Descendants of Immigrants*. This is a fine service. As he says "a great many questions relating to heredity and environmental influences may be treated by means of this material."

FACTORS THAT INFLUENCE WOOL PRODUCTION WITH RANGE RAMBOUILLET SHEEP. *United States Department of Agriculture Technical Bulletin No. 85.*
By D. A. Spencer, J. I. Hardy and Mary J. Brandon. *U. S. Government Printing Office*
15 cents *Washington, D. C.*
6 x 9⅛; 48 (paper)

An investigation of the relations of age, body weight, mutton type, face covering, and skin folds to the amount and quality of fleece in Rambouillet sheep. The results as here presented are chiefly of interest to wool producers; whether more adequate statistical analysis of the original data would yield anything of biological interest we cannot say.

DIE CYTOLOGISCHEN GRUNDLAGEN DER VERERBUNG. *Handbuch der Vererbungswissenschaft Band I, Lieferung 5.*
By Karl Bělař. *Gebrüder Borntraeger*
80 marks *Berlin*
Subscription price 40 marks
7 x 10½; iv + 412 + 2 plates (paper)

This section of the Baur-Hartmann handbook of genetics is a thorough and detailed review of the cytological basis of heredity. The successive chapters deal with cytomorphology; nuclear and cell division; cell differentiation; fertilization; parthenogenesis; chromosome reduction; individuality of chromosomes; chromosomes and heredity (crossing-over, etc.); cytoplasm and heredity. There is a bibliography of 32 pages. A useful section of a valuable reference work.

THE CYTOLOGY OF OENOTHERA.
By R. Ruggles Gates. *Martinus Nijhoff*
6¼ x 9⅝; 92 (paper) *The Hague*

This well illustrated review contains a table giving the chromosome numbers in the species and mutants of *Oenothera*, with

the authors and dates, up to the end of 1927. There is a lengthy list of references and an index.

GENERAL BIOLOGY

WHAT IS LIFE?

By Augusta Gaskell (Introduction by Karl T. Compton and Raymond Pearl).

Charles C. Thomas

$3.50 6¼ x 9¼; 324 *Springfield, Ill.*

From time to time there have been noticed here biological and philosophical works of the paradoxical kind which delighted Augustus De Morgan. If we were to give a bare statement of Mrs. Gaskell's theory, most of our readers would probably place her in that class. But we can assure them that she is no paradoxer; one may not be converted by her argument, but that she is a thoroughly sane person with a keen and logical mind cannot be doubted by anyone who will read the book.

Essentially her theory postulates that under certain conditions protons and electrons combine to form new, intra-atomic units, which, it is assumed, form the essential ingredients of living matter; and that these combine with ordinary elements to form living matter, which is thus a "dual" system. From this starting point, she proceeds to the interpretation of various life phenomena.

The first question, of course, will be as to the possibility of this sort of system. Professor K. T. Compton, in his introduction says:

> The author's answer to the question "What is Life" purports to be based on the facts of modern atomic physics. The first query that will naturally occur to the serious reader is in regard to the author's qualifications in the field of physics. To this I would say that her discussion of modern atomic physics is accurate, well balanced and worth reading for its own sake.
>
> The honest physicist must admit that he knows no independent experimental evidence to suggest or support the hypothesis of these assumed "Z" combinations of protons and electrons. He must also admit that he really knows relatively very little about atoms, protons and electrons, and nothing at all about the explanation of life. Hence the author's fundamental assumption must be admitted as possible. Further, she has shown how it can be used as a working hypothesis in a variety of directions. Finally, it should be susceptible of experimental test. These considerations should support the author in her plea for serious consideration of her work on its merits as a stimulus towards an experimental test of her theory.

We suggest that before dismissing the book as harmless lunacy, it be read; it is quite imaginable that it may suggest some new and valuable ideas.

MORPHOLOGIC VARIATION AND THE RATE OF GROWTH OF BACTERIA.

By Arthur T. Henrici. *Charles C. Thomas*

$3.00 6 x 8½; xiii + 194 *Springfield, Ill.*

This first volume of a new series of Microbiology Monographs, edited by R. E. Buchanan, E. B. Fred and S. A. Waksman, presents the results of a statistical study on the cell changes of bacteria in growing cultures. The author makes no claim to being an expert in biometry but nevertheless even with the application of simple statistical methods he has obtained results of real significance. He shows that

> contrary to the orthodox teaching, the cells of bacteria are constantly changing in size and form and structure; but that instead of these changes occurring in a haphazard or meaningless fashion, or instead of being phases in a rather vague and complex life cycle, they occur with great regularity and are governed by relatively simple laws which, after more data have been accumulated and analysed, may probably be very precisely formulated.

The results indicate that the growth of these organisms is governed by the same laws which govern the growth of multicellular organisms—that there is a period of rapid growth in an early stage of development, a period of slow growth or rest in the mature form, and in the senescent form the period of death.

In the text there are 36 figures and 2 plates. There is an appendix containing 27 tables exhibiting rate of growth of the bacterial cultures, also one containing a list of references. There are also author and subject indices. We congratulate the publisher on having inaugurated this new series of monographs with a volume so auspicious in respect of both scientific content and book manufacturing.

GILBERT WHITE. *Pioneer, Poet, and Stylist.*
By Walter Johnson. *John Murray*
15 shillings net $5\frac{1}{2}$ x $8\frac{5}{8}$; xvi + 340 *London*

An account of the life and work of one of the most interesting of English naturalists. Gilbert White was one of those English curates of the eighteenth century—the breed, we hope, is not extinct—whose real interest lay in the world about them rather than in that above them. Throughout his seventy odd years of life he observed nature and his fellows, the world and its inhabitants, as he saw them in his Hampshire village of Selborne. His work has retained its fascination for a century and a half.

The present volume attempts to estimate the value of White's work, both on its scientific and literary sides. The author has, we feel, done some unnecessary apologizing for his hero; some of the accusations which he refutes seem not worth noticing. As for his estimate of White's scientific work, we doubt that all his claims could be fully substantiated. It is easy to pick a sentence from an early writer, and show that this indicates that the author really had the very latest modern discovery in mind, if he had only gone on to work it out. We rather think that it would be easy for an ingenious Jesuit to show by this technique that Saint Thomas Aquinas knew all about natural selection. However, we are quite willing to let the point pass; if this book persuades a few more people to look into *Selborne*, it will have accomplished its purpose.

NEW ESSENTIALS OF BIOLOGY. *Presented in Problems.*
By George W. Hunter. *American Book Co.*
$1.68 $5\frac{1}{4}$ x $7\frac{7}{8}$; x + 453 *New York*
NEW LABORATORY PROBLEMS IN CIVIC BIOLOGY.
By George W. Hunter. *American Book Co.*
96 cents $7\frac{1}{2}$ x $9\frac{1}{2}$; 286 (paper) *New York*

These texts have, we assume, the approval, if not the explicit *imprimatur*, of Dr. Clarence True Wilson, Dr. John Roach Straton, and Bishop James Cannon. At least they should have. They have clearly been written with the statutes of Tennessee and Arkansas in mind, as well as the clip sheet of the Methodist Board of Temperance, Prohibition, and Public Morals. The word "evolution" has been carefully omitted from the index, and we have not found anything in the book which a Baptist Sunday School teacher could not reconcile with Genesis. We are also pleased to note the author's desire to give offense to no one by carefully referring to "the early settlers in Utah" rather than to the Mormons.

As an illustration of the care which has been taken to provide conclusive experimental evidence to substantiate the state-

ments made in the text, we quote from the Laboratory Problems:

> Problem: To Determine the Effect of Alcohol upon Raw White of Egg.
>
> Materials.—White of egg. Alcohol. Test tubes.
>
> Note.—In chemical and physical composition the white of egg is nearly like protoplasm.
>
> Method and Observations.—Pour into a test tube a small amount of raw white of egg. Pour slowly a little alcohol into the tube. What effect does it have on the white of egg? Pour in equal amounts of alcohol and of egg, and mix the two substances by shaking. What is the effect?
>
> Conclusions.—1. How does alcohol affect the white of egg?
>
> 2. Might it have the same effect on living matter?
>
> Note.—The action of alcohol is to take out the water from the white of egg.
>
> Questions.—1. What is an adulteration? Does your pure food law protect you from adulteration of food?
>
> 2. Is alcohol a food? Is it a poison? Can any material be both a food and a poison?

GROWTH.

By William J. Robbins, Samuel Brody, Albert G. Hogan, Clarence M. Jackson and Charles W. Greene. *Yale University Press*

$3.00 6 x 9; xiii + 189 *New Haven*

These are five essays on various aspects of growth by associates of the University of Missouri, as follows: Introduction, by William J. Robbins; An Analysis of the Course of Growth and Senescence, by Samuel Brody; Some Relations between Growth and Nutrition, by Albert G. Hogan; Some Aspects of Form and Growth, by Clarence M. Jackson; Physiological Factors Regulating Normal and Pathological Growth, by Charles W. Greene. For the most part they are brief reviews of the elementary facts relating to the subjects discussed. The article by Brody attempts a profounder analysis, being in essence an attempt to obtain mathematical generalizations that will take in the entire aging process; it is however basically unsound on the mathematical side.

There is a great need for a work which will synthesize comprehensively what is known regarding growth and crystallize the outstanding problems demanding further study. This book is not that work.

THE PRINCIPLES OF SYSTEMATIC ENTOMOLOGY. *Stanford University Publications. University Series. Biological Sciences Vol. 5, No. 3.*

By Gordon F. Ferris.

Stanford University Press

$2.00 (paper) *Stanford University*

$2.75 (cloth)

7 x 10; 169

This critique of systematic entomology is a valuable contribution to biological literature. After an introductory chapter on the contribution of the systematist to biology, there follows a discussion of the principles of systematic entomology, at the conclusion of which are listed eight theses which the writer defends not only as conforming to the theoretical requirements of systematic entomology but also as admitting of an adequate degree of attainment in practice. The remainder of the book is concerned with a comprehensive discussion of these principles and the methods by which they may be applied. Included in the section on "Nomenclature" is a reprint of the International Code. There are a number of illustrations in the text, and an index is appended.

ÉLÉMENTS DE BIOLOGIE GÉNÉRALE.

By Étienne Rabaud. *Félix Alcan*

45 francs $5\frac{3}{4}$ x 9; xv + 478 (paper) *Paris*

A philosophical (and therefore necessarily wordy) consideration of general bi-

ology, which the author describes as follows:

> General biology is therefore neither morphologic nor physiologic; it begins with concrete facts which a precise and certain analysis furnishes it, to end with a knowledge of the relative value and deeper significance of vital phenomena.

The book is well informed, penetrating in its analysis of the methodology of biological science, and makes profitable but, because of the poor print, uncomfortable reading. A table of contents is to be found at the end of the book, but no index.

LA VIE.
By Jean-Paul Bounhiol. Ernest Flammarion
12 francs net 4¾ x 7¼; 330 (paper) *Paris*

An interesting attempt at a synthetic envisagement of all the phenomena of biology from the point of view of energetics. The author is a thorough going mechanist, who believes that the excess of attention which has been paid to morphology has had a retarding effect upon the progress of biological philosophy. He thinks that the essence of life lies in the catalytic oxidation of complex colloids in an aqueous medium. He knows the literature of biology well, and has produced an interesting book, well worth reading even if a bit one-sided.

THE HISTORY OF BIOLOGY.
By Erik Nordenskiöld (Translated from the Swedish by Leonard B. Eyre).
Alfred A. Knopf
$6.00 6¼ x 9½; xi + 629 + xv *New York*

An English translation of this excellent work, the German edition of which was noticed here in Volume I, Number 4. In its present form it has been much improved by the addition of illustrations and by the enlargement of the index. Author, translator, and publisher may well feel satisfaction in the book.

LEHRBUCH DER EXPERIMENTAL-ZOOLOGIE. *2. Auflage. Teil 1 und 2.*
By Bernhard Dürken. Gebrüder Borntraeger
51 marks (paper) 7 x 10¼; xii + 782 *Berlin*
54 marks (cloth)

The second edition, revised and enlarged, of a standard textbook of experimental embryology, in which emphasis is placed upon the correlation and synthesis of the results of genetics and *Entwicklungsmechanik*. There is a bibliography of some 60 pages, and a detailed index.

EINFÜHRUNG IN DIE BIOLOGIE DER SÜSSWASSERSEEN.
By Friedrich Lenz. *Julius Springer*
12.80 marks (paper) *Berlin*
14 marks(cloth)
6½ x 9½; viii + 221

This treatise on the biology of lakes is a welcome addition to the literature, and well maintains the high standard set in earlier numbers of the series of *Biologische Studienbücher*, of which it is the ninth. The approach is ecological throughout. There is a selected bibliography covering 6 pages, and an index.

METHODIK DES BIOLOGISCHEN UNTERRICHTS. *Ein Hilfsbuch für Lehrer aller Schularten. Teil II: Didaktische Skizzen und Lebensbilder.*
By Karl Smalian. *Otto Salle*
16 marks (cloth) 6 x 9; xii + 282 *Berlin*
14.50 marks (paper)

A handbook of pedagogical technique

for the teacher of elementary biology and nature study. Its point of view is that of natural history. Anyone who is attempting anything in the way of field work with his students will find this book helpful. It is abundantly illustrated.

LIFE IN INLAND WATERS *with Especial Reference to Animals.*
By Kathleen E. Carpenter. The Macmillan Co.
$4.50 5½ x 8½; xviii + 267 *New York*

A treatise on fresh-water biology, with especial reference to animals, prepared for the use of British students. The standpoint of the work is ecological. The book is fairly well illustrated and has both author and subject indices. At the end of each chapter is a list of references, frequently of considerable length.

DER SAUERSTOFF IM EUTROPHEN UND OLIGOTROPHEN SEE. *Ein Beitrag zur Seetypenlehre.*
By August Thienemann.
E. Schweizerbart'sche Verlagsbuchhandlung
18 marks (paper) 6⅝ x 10; 175 *Stuttgart*
19.50 marks (cloth)

A highly special piece of research and review of the literature on the types of freshwater lakes, with special reference to the oxygen content of the water. It constitutes the fourth volume of a series on limnology, under the general title *Die Binnengewässer.* There is a bibliography covering 3 pages.

DER NATURFREUND AM MEERESSTRANDE. *Eine Einführung in das Verständnis für das Meer.*
By Carl I. Cori. *Emil Haim und Co. Vienna*
9 marks 5¼ x 7¾; xi + 174 + 22 plates

This little book aims to serve as an introductory guide for nature classes interested in life forms of the seashore. For a popular book it seems rather heavy, and the poor print and sparsity of illustrations aggravate the impression that it is not well suited to the purpose for which it was intended. There is a list of references and an index.

A BRIEF COURSE IN BIOLOGY.
By Walter H. Wellhouse and George O. Hendrickson. *The Macmillan Co.*
$1.80 5⅛ x 7¾; xii + 200 *New York*

Designed as a text for a half year introductory course in general biology. It is brief indeed and suffers from didacticism.

DAS LEBEN DER WOLGA. *Zugleich eine Einführung in die Fluss-Biologie.*
By Arvid Behning.
E. Schweizerbart'sche Verlagsbuchhandlung
17.50 marks (paper) *Stuttgart*
19 marks (cloth)
6½ x 9¾; vi + 162

This serves both as an introduction to the general subject of potamobiology and as a specific consideration of biological forms in the Volga River.

HUMAN BIOLOGY

THE SHADOW OF THE WORLD'S FUTURE. *Or the Earth's Population Possibilities and the Consequences of the Present Rate of Increase of the Earth's Inhabitants.*
By Sir George H. Knibbs. *Ernest Benn Ltd.*
10s. 6d. net 5½ x 8½; 131 *London*

THE BALANCE OF BIRTHS AND DEATHS. *Volume I, Western and Northern Europe.*
By Robert R. Kuczynski. The Macmillan Co.
$2.00 5 x 7⅜; xi + 140 *New York*

About the only point of agreement between the authors of these two books is that they are both viewers-with-alarm. Otherwise they are as completely different as any two books on the population problem could be. One is a careful and detailed study of a particular demographic problem; the other is an emotional outpouring of uplift and bad logic.

Sir George Knibbs, we are bound to say, has disappointed us. We had expected that the first Statistician to the Australian Commonwealth would have given us a reasoned scientific argument. We find, however, very little reason or science in the book. He is greatly disturbed over the tremendous increase in population during the last century; and he thinks something must be done about it. We find some of his reasoning about the rapidity with which we are approaching the saturation point (which he puts at from 5,200 to 11,000 millions) a little dubious; while on the other hand we can hardly assent to some of his arguments for putting the saturation point as high as he does. But the book on almost every page shows that it was written less as science than as propaganda, and that logic was an unimportant consideration when it traversed emotional prejudices. A few quotations will perhaps substantiate this statement.

> The studies of racial characteristics, of the possibilities of beneficient human intercourse, of the problems of miscegenation, of a better personal, communal, national and international hygiene, of eliminating or ameliorating the more terrible diseases and scourges of mankind, of international economics, and of international relations generally, would all become financially possible were war assuredly obsolete.

> When a people, having become subject to a control which has actually destroyed enormous numbers of them, a control which also has plunged them into economic ruin, endeavours by all sorts of subterfuges to spread its political creeds among other peoples, it makes a national goodwill to it fatuous, hinders economic relationships with it, and renders mutual migrations impossible.
>
> The fact that the uses and applications of capital are not associated with particular persons, nor are they collateral with particular nationality, has also shown that the economic organisation of the world is, at present, very unsatisfactory.

Turning from Sir George Knibbs and his fears, let us say a few words with regard to Kuczynski's study. He has concerned himself with the problem of determining whether the population of Western Europe is really maintaining itself; that is, whether the mothers of the present time are actually reproducing themselves. By a comparison of age-specific fertility and mortality rates he finds that:

> According to the fertility and mortality in Western and Northern Europe in 1926, 100 mothers give birth to 93 future mothers only. With the fertility of 1926 the population is bound to die out unless mortality of potential mothers decreases beyond reasonable expectations. And fertility continued its downward path in 1927.

This problem is, of course, the same that was studied for the United States by Dublin and Lotka. Whether such a conclusion as Kuczynski's or the but slightly more favorable (in the numerical sense) conclusion of Dublin and Lotka, is really cause for great concern is something else again. For our own part, we are inclined to accept it as Margaret Fuller did the universe. But we recommend the book to Sir George Knibbs whenever he is particularly worried about how to feed the 11,000 millions of people who agitate him so.

STUDIES IN THE NATURE OF CHARACTER *by the Character Education Inquiry, Teachers College, Columbia University in Cooperation with The Institute of Social and Religious Research. I. Studies in Deceit. Book One, General Methods and Results. Book Two, Statistical Methods and Results. By Hugh Hartshorne and Mark A. May.* *The Macmillan Co.*
$4.50 *New York*
5 x 7¾; xxi + 414 + vii + 306

An investigation of the factors related to dishonest behavior in school children. The results of tests devised to give children an opportunity for cheating without apparent danger of detection are here presented at length. The book is not easy reading, but contains some interesting matter. In particular, the evidence indicates that the influence of the individual teacher is of greater importance than the use of "progressive" or "traditional" methods of instruction—a conclusion which does not surprise us, but which may distress "progressive" educational theorists.

With regard to specific attempts to "build character," some interesting evidence is submitted.

> The organization we shall call system X is a device for interesting school children in the achievement of virtues through practice. When we encountered this scheme, each child was expected to keep a daily record of certain good deeds (among which was truth telling); and, to stimulate him in his effort and so make sure that each virtue was properly practiced, he was rewarded for a good record by being advanced in the organization from rank to rank.

The results of exposure to this influence are not such as to encourage faith in its efficacy. It was found that the longer a pupil was exposed to the system, the more he cheated. And for Sunday schools:

> We may say that neither the length of time that children are associated with Sunday school nor the regularity of their attendance seems to be at all associated with their tendency to deceive either at school or on work taken home.

Again, the effects of another system (which we guess to be one of the Boy Scout organizations) are commented on as follows:

> The numbers on which these three studies of system Y have been based are of course too small to warrant broad generalizations concerning the organization as a whole; and its sponsors, moreover, say that it is not at its best in the communities from which our cases come. We can only conclude that in these places this widely used agency for moral education, whatever its effect may be elsewhere, is either neutral or deleterious with regard to one of its major aims, the teaching of honesty. This conclusion must be at once supplemented, however, for system Y as for system X and the religious schools, by the caution that in other ways it may be having a vast influence for good.

DIGHTON ROCK. *A Study of the Written Rocks of New England.*
By Edmund B. Delabarre. *Walter Neale*
$6.00 6 x 9¼; xv + 369 *New York*

Although the title of this interesting book is "Dighton Rock," the author has included in his discussions other famous rocks in New England where puzzling drawings and inscriptions have been found. Much of the material has already appeared in special articles. Here are presented the more important features of these in a more compact form, with revisions and additions, as the study has progressed.

There are three centers in New England at which aboriginal rock-carving occurred —the most important of these being the region about Narragansett Bay, where it has been found in from fifteen to twenty separate localities. These have been ascribed to many sources, beginning with possible early Phoenician explorers down

to Miguel Cortereal, the Portuguese explorer, who lived in this region about 1511. The first inscriptions on Dighton Rock the author believes go back to the intrepid Cortereal, who, wishing to attract the attention of possible explorers, recorded, among other things, that he was the leader of the local Indians. Additions were probably made at a later date by other early settlers, and the Indians soon followed their example with numerous carvings on rocks and stones in the Narragansett and Machias regions, but rarely elsewhere in New England. For the most part there is no evidence to indicate that the Indian carvings had any significance.

By no means the least interesting feature of this book is that it is the outgrowth of research done during vacation periods by one who by profession is a teacher of psychology. The book is well illustrated and contains a lengthy bibliography and an index.

THE GROWTH OF MANUFACTURES 1899 to 1923. *A Study of Indexes of Increase in the Volume of Manufactured Products. Census Monographs VIII.*
By Edmund E. Day and Woodlief Thomas. *U. S. Government Printing Office*
$1.35 7 x 10; 205 *Washington, D. C.*

The authors present an analysis in detail and combine their individual results into synthetic estimates of the growth of manufactures in this country over the period 1899 to 1923.

The importance of this sort of work for the study of broad problems in human biology has not been duly recognized. In the discussion of population and eugenic questions that one finds in the current literature, there is blithe disregard of the fact that these matters cannot be intelligently considered except in terms of multiple complex factors. No absolute standards for population are statable, either as regards total numbers or differential qualities. In biometric terms what we require are multivariate equilibrium equations that will give optimal values for one social variable in terms of given values of others. Until considerable progress is made in the development of such equations, the significance of specific changes that are noted in population trends cannot be estimated. As examples of this we may cite the work of Pearl and the study of Pitkin in *The Twilight of the American Mind*, on the import of existing population trends. Both reach conclusions directly opposed to those usually stated, because they take into account industrial and economic changes. It is from this point of view that we regard the sort of data given in the work reviewed as of fundamental importance for human biology.

GEOGRAPHY OF AMERICAN NOTABLES: *A Statistical Study of Birthplaces, Training, Distribution: An Effort to Evaluate Various Environmental Factors. Indiana University Studies Vol. XV, No. 79.*
By Stephen S. Visher. *University Bookstore*
75 cents $5\frac{7}{8}$ x 9; 138 (paper) *Bloomington*

This is a statistical study of the birth places, training and distribution of various sorts of American notables, and an attempt at an evaluation of the various environmental factors. The material was taken from the starred names in Cattell's *American Men of Science*, and from *Who's Who in America*. Among other glimpses of the obvious are these:

"A region which leads in producing important types of leaders also holds a similar rank in producing other sorts of leaders, and in other significant evidences of merit;" "In the United States there is a southward

decline among the states in the productions of almost all types of leaders in proportions to populations, and in most other evidences of social merit;" "The rank of an area depends not primarily upon fixed environmental conditions such as climate, topography and soil but upon the character of the predominant population".

The author also finds that cities and towns are more favorable for producing notables than are rural communities; "that a small proportion of men father a large share of notables;" that there is a "close correlation between enthusiasm for research on the part of college professors and output of students who later merit starring," that "for graduate training the leaders here studied have gone largely to a few strong institutions which have on their faculties many notable men;" and that "there is a notable and increasing concentration of the starred scientists in a relatively few institutions situated in a few states." Thirty-one tables and ten figures exhibit the statistical data.

QUANTITATIVE METHODS IN POLITICS.

By Stuart A. Rice. *Alfred A. Knopf*
$3.00 $5\frac{3}{8}$ x 8; xxii + 331 *New York*

This book should furnish entertaining reading to the statistically minded. The author has attempted to answer various questions in regard to political behavior by the application of statistical methods. Usually he ends by pointing out that the question is still unsettled. The book, however, indicates that there exists a large field for the statistical treatment of political data, with the possibility of drawing interesting conclusions with regard to human behavior and attitudes.

With regard to the statistical techniques employed, it is to be noted that they are largely devised by the author for the solution of particular problems; and that, while some of them are obviously open to damaging criticism, they are interesting and stimulating to the statistician. They evidently need improvement; but so did the correlation coefficient in the original form in which Galton used it.

But why the attribution to Professor Truman L. Kelley of the Pearsonian frequency curves?

AINU LIFE AND LORE. *Echoes of a Departing Race.*

By John Batchelor. *Kyobunkwan*
$6.00 post free $6\frac{1}{4}$ x 9; viii + 448 *Tokyo*

Having lived since 1879 as a missionary among the Ainu, the author has had a remarkable opportunity for observing and recording the customs, language and folklore of this fast disappearing race, which in ancient times probably occupied all of Japan. Reduced now in numbers to about 15,000, and living only in the north, in Hokkaido and Saghalien, they seem to have held closely to their ancient traditions and preserved many of their legends in spite of the fact that adoption of Japanese children has in past ages been one great way of keeping up the numbers of the race. Without it, the author states, the Ainu would have been extinct long ago. This would seem to indicate that very few pure types are now in existence, and probably accounts for some of the diverse types exhibited as Ainu in the photographs of this book. The writer finds much in their language that points to an Aryan ancestry, in both the vocabulary and the grammar. The most striking thing about the men is the very thick and sometimes quite long hair and heavy moustache. One of the niceties of table etiquette is the use of the moustache lifter

—especially artistic ones being provided for ceremonial occasions.

The book contains numerous illustrations, mostly photographs or reproductions from water-color drawings by Ainu and Japanese artists. There is no index.

AMERICAN MARRIAGE AND FAMILY RELATIONSHIPS.

By Ernest R. Groves and William F. Ogburn.
Henry Holt and Co.
$4.50 5½ x 8½; xiii + 497 *New York*

This admirable treatise on the institution of marriage as it exists in America today and the resultant behavior of the individuals concerned, will be of interest to students and educators as well as to the general reader. Professor Ogburn contributes a comprehensive statistical study of the subject, which furnishes a sound basis for future work in this line. Upon Professor Groves has devolved the task of gathering the evidence from a study of case histories of happy as well as unhappy marriages, and of evaluating the many tendencies and efforts of those of the present era to depart from the orthodox manner of living which was in vogue when we were young. He does this with a fine sense of judgment. A final section is devoted to a study of correlations, for the benefit of those who wish to study the application of the statistical method to the solution of social problems.

There is a general bibliography on marriage and a special bibliography of the census publications in this field.

A STUDY OF REHABILITATED PERSONS. *A Statistical Analysis of the Rehabilitation of 6,391 Disabled Persons. Bulletin No. 132. Civilian Vocational Rehabilitation Series No. 16.*

Issued by the Federal Board for Vocational Education. U. S. Government Printing Office
10 cents *Washington*
5⅞ x 9⅛; ix + 46 (paper)

Our bilious view of tax-supported activities has often distressed our forward-looking friends. The present pamphlet introduced us to a new device for keeping up our income tax which we had somehow overlooked. It appears that there exists a Federal Board for Vocational Education, which publishes bulletins now numbered up to 132, and whose activities include co-operative spending of money with the states for vocational rehabilitation of disabled persons. This bulletin purports to analyze the results of the work accomplished during the years 1920–1924.

Unfortunately, it is impossible to determine from the report what has been accomplished. If we take the report at its face value, it would appear that the average earnings had increased from less than $10 per week after injury but prior to rehabilitation to more than $20 per week at the time of interview; and that the cost had averaged less than $150 per case. Matters are not as simple as this, however, for we are given no information whatever on which to form an estimate of how much the rehabilitation service had to do with all this. We do not know the nature of the injury in relation to the job held; we do not know the relation of the cost of rehabilitation to the wages before and after rehabilitation; we do not know the true cost of the rehabilitation work (since overhead has been omitted from the figures given); in fact we know nothing of real value in regard to the whole business.

THE AGE OF THE GODS. *A Study in the Origins of Culture in Prehistoric Europe and the Ancient East.*
By Christopher Dawson. Houghton Mifflin Co.
$5.00 5½ x 8⅝; xx + 446 *Boston*

We are witnessing the rise of a new science which will study man's past, not as an inorganic mass of isolated events, but as the manifestation of the growth and mutual interaction of living cultural wholes. . . . . During the last two centuries the history of Europe has been given an almost exclusively national interpretation. And since the unit is a political one, the method of interpretation has tended to be political also. . . . . Now the alternative to the nationalist conception of history is the cultural or sociological one, which goes behind the political unit and studies that fundamental social unity which we term a culture.

With this *Anschauung* the author traces the history of cultural progress, especially as it has been revealed in the last three decades of archeological and ethnological research. It begins with the glacial age and the paleolithic periods and extends through the iron age in Italy, forming an interesting if somewhat compact synthesis of our knowledge of the development of civilization during this long interval. The book is supplied with a bibliography, chronological tables and an index.

THE ALCOHOL PROBLEM.
By H. M. Vernon. Baillière, Tindall and Cox
9 shillings 5½ x 8½; xv + 252 *London*

The author attempts a survey of the experience of man with the consumption of alcoholic liquors and its control through legislation. He believes some sort of control is necessary but is otherwise disinterested and looks to the securing of a body of knowledge which will permit a wise solution of the problem as it exists in England. The history and effects of prohibition in the various countries where it has been tried are reviewed, as well as the experimental and statistical studies that have been made to determine the vital effects of imbibition. Unfortunately as regards the experience with prohibition the statistics are not brought up to date so that important trends over the last five years are not given. The references provided are limited to works cited; there is an index.

SCIENCE AND GOOD BEHAVIOR.
By H. M. Parshley. The Bobbs-Merrill Co.
$2.50 5¼ x 8; 281 *Indianapolis*

This is a good and a courageous book, but Quixotic. Professor Parshley is much too intelligent a person not to know that the criteria of "good" behavior, as they exist and are accepted in this world as it is here and now constituted and operated, have little indeed to do with such things as science, reason, or even common decency, we regret to say. What he does in this book is to outline his conception of a *rational* system of ethics, based upon present knowledge of general and human biology. The result is interesting and stimulating. Reginald, the office boy, says that Professor Parshley is just another kind of uplifter. But Reginald is young, and therefore harsh. A more constructive criticism, we think, is to suggest that Parshley read and ponder over Pareto's *Traité de Sociologie Générale.*

MYSTERIES OF HISTORY *with accounts of some remarkable characters and charlatans.*
By C. J. S. Thompson. J. B. Lippincott Co.
$4.00 5⅛ x 8½; 319 *Philadelphia*

A well-done piece of literary composition, with a good deal of interest in it for the biologist. Mary Toft, who gave birth to rabbits, or at any rate said she did, was an entertaining person. So also was Franklin's friend James Graham, a

high-toned quack whose "Celestial Bed" was a noble idea. At a charge of 450 guineas per night it could be occupied for the purpose of engendering "children of the most perfect beauty." It was *some* bed. This is a book to read along with *Oddities*, noted in this number

LIVELIHOOD IN PEKING. *An Analysis of the Budgets of Sixty Families.*
By L. K. Tao.
Social Research Department, China Foundation for the Promotion of Education and Culture
$3.00 (cloth) *Peking*
$2.00 (sewed)
6½ x 9½; 158 + xxii

An investigation of living expenses among the poorer classes in Peking, based on account-books for 48 families over six months, and 12 elementary school teachers for a month. It is interesting to note that out of 72 employed males in the 48 families, 41 were rickshamen. It appears from the report that this proportion is not unreasonable in a sample of this size and economic status. The report will be of considerable interest to anyone desiring some idea of the living conditions of the poorer classes of Chinese.

RACE AND CIVILIZATION.
By Friedrich Hertz. *The Macmillan Co.*
$7.50 5½ x 8⅝; xii + 328 *New York*

A counterblast to the Nordics. Dr. Hertz makes noble play with Gobineau, Chamberlain, Fischer, Grant, Stoddard, *et al.* Not the least amusing part of the book is that in which he shows how Grant and Stoddard, having borrowed the Nordic dogma from the German race theorists, proceed to show that the Germans are really not Nordic at all. In Dr. Hertz's words "he steals the clothes of German race theorists, alleging that these clothes did not rightfully belong to them."

We recommend the book heartily to anyone who needs a purgative after a dose of Nordicism. We are not prepared to guarantee all the kind words the author has for the inferior races, but he has successfully demolished most of the claims for race superiority. The book badly lacks an index.

IMMIGRATION AND RACE ATTITUDES.
By Emory S. Bogardus. D. C. Heath and Co.
$1.80 5⅛ x 7¾; xi + 268 *Boston*

Here we have another book on the "greatest issue confronting us," this time race relationships. The author strives at scientific objectiveness by employing the answers to questionnaires on race attitudes prepared for the purpose, as the basis of his analysis. Through this medium he discovers the origin of race antipathy, its modes of perpetuation, and how adjustment may be accomplished. The book is apparently designed as a classroom text and contains a list of "projects" and references at the end of each chapter.

IMPRESSIONS OF GREAT NATURALISTS. *Darwin, Wallace, Huxley, Leidy, Cope, Balfour, Roosevelt, and Others.*
By Henry Fairfield Osborn.
Charles Scribner's Sons
$2.50 5¼ x 7½; xi + 294 *New York*

This is a second and revised edition of Professor Osborn's entertaining collection of biographical sketches of great biologists. To the beginning student of any branch of natural history this volume

will be an inspiration. To the oldster it is a refreshing reminder of the giants who broke out the main pathways for him. One infers from a somewhat cryptic footnote that Professor Osborn is about to publish a definitive biography of Cope. In the hope that this is a correct inference we await this volume with the keenest interest, for Edward Drinker Cope was, beyond question, the most brilliant biologist that America has ever produced.

A BIBLIOGRAPHY OF ALASKAN LITERATURE 1724–1924. *Vol. 1. Miscellaneous Publications of the Alaska Agricultural College and Schools of Mines.*
By James Wickersham.
Cordova Daily Times Print
$5.50 *Cordova, Alaska*
$5\frac{3}{4}$ x 9; xxvii + 635

A bibliography of 10,380 titles, which are supposed to constitute "a complete list of the titles of all printed books of history, travels, voyages, newspapers, periodicals, and public documents, in English, Russian, German, French, Spanish, etc., relating to, descriptive of, or published in Russian-America, now called Alaska, from 1724 to and including 1924."

OFFICIAL VITAL STATISTICS OF SWITZERLAND. *Statistical Handbook Series: No. 12. Publications of the League of Nations. III. Health. 1927. III. 16.*
World Peace Foundation
60 cents $7\frac{1}{4}$ x $9\frac{1}{2}$; 88 (paper) *Boston*

This report is No. 12 of the *Statistical Handbook Series*, issued by the Health Organization of the League of Nations. The previous issues describe the official vital statistics of the following countries: the Netherlands, Belgium, England and Wales, Spain, Austria, Czechoslovakia, France, Hungary and Italy. These handbooks are extremely useful to the student of human biology, as they give in detail the precise methods of collection and tabulation of vital statistics in the several countries.

FINANCIAL STATISTICS OF CITIES HAVING A POPULATION OF OVER 30,000. 1926.
By Department of Commerce, Bureau of the Census. U. S. Government Printing Office
$1.25 (buckram) *Washington*
$5\frac{7}{8}$ x $9\frac{1}{4}$; 505

A melancholy tabulation showing where the taxpayer gets hit and why. The sad tale shows per capita tax receipts rising from $21.14 in 1903 to $66.14 in 1926. The one encouraging feature shown is an apparent tendency to increase the proportion of payments made from revenue as against that from funded debt.

L'ART DE CONNAÎTRE LE CARACTÈRE PAR LA PHYSIONOMIE.
By Jean Lefas. *Norbert Maloine*
30 francs $6\frac{1}{4}$ x 9; 326 (paper) *Paris*

A French treatise on physiognomy. We cannot see that it possesses any advantages for English-speaking readers over the scientific treatises of Dr. Katherine Melvina Huntsinger Blackford.

STUDIES IN HEREDITARY ABILITY.
By W. T. J. Gun.
George Allen and Unwin, Ltd.
10 s. 6 d. $5\frac{3}{8}$ x $8\frac{1}{2}$; 288 *London*

This discussion of the family histories of certain well known British and American families will be of much interest to

the general reader who likes to delve into genealogical literature. The serious student of heredity will require a more complete record of data than is here presented, and a more critical analysis of such material.

THE OPPOSITE SEXES. *A Study of Woman's Natural and Cultural History. By Adolf Heilborn (Translated from the German by J. E. Pryde-Hughes).*

Methuen and Co., Ltd.
6 shillings net *London*
$4\frac{3}{4}$ x $7\frac{1}{2}$; viii + 152

A consideration of the physical structure, psychology, and social position of woman, uncritically written and of slight importance. It does not compare in value with Havelock Ellis's *Man and Woman*.

WHAT IS EUGENICS?
By Major Leonard Darwin. *Watts and Co.*
1 s. net $4\frac{3}{4}$ x $7\frac{1}{4}$; viii + 88 *London*

A brief statement, gotten out for the popular Forum Series, of the matters discussed by the author at greater length in his *The Need for Eugenic Reform*, which has been commented on in this REVIEW (Vol. I, No. 4).

ZOOLOGY

VERTEBRATE ZOOLOGY. *An Introduction to the Comparative Anatomy, Embryology, and Evolution of Chordate Animals. By G. R. de Beer.* *The Macmillan Co.*
$5.50 $5\frac{1}{2}$ x $8\frac{1}{2}$; xx + 505 *New York*

In this introduction to the comparative anatomy, embryology, and evolution of chordate animals, the author devotes the first two parts to the study of types. In Part I, *Amphioxus*, *Petromyzon*, *Scyllium*, *Gadus*, *Ceratodus*, *Triton*, *Lacerta*, *Columba*, and *Lepus* are chosen for a study of adult structure; while in Part II, *Amphioxus*, *Rana*, *Gallus* and *Lepus* are used as embryological types. Part III is devoted to a comparative treatment of the various organ systems. This forms the largest section of the book. With the types presented in the first two parts forming a framework, the author introduces in this section other animals, which contribute much that is essential for a logical development of the subject. Part IV is devoted to a discussion of evolutionary morphology. This method of developing the study of the chordate group has much that is commendable. The author has succeeded in discarding many details which are unessential in a general survey and are confusing.

At the end of each chapter there is a brief list of references. There are 185 illustrations within the text, while the volume is completed by a section giving the classification of the animals and groups of animals mentioned, and an index.

Professor Julian Huxley contributes an introduction.

A CONTRIBUTION TOWARD A MONOGRAPH OF THE ADELGINAE (PHYLLOXERIDAE) OF NORTH AMERICA. *Stanford University Publications, Biological Sciences Vol. VI, No. 1. By P. N. Annand.* *Stanford University Press*
$2.00 (paper) *Stanford University*
$2.75 (cloth)
7 x 10; 146

This work on the Adelginae of the United States is a valuable contribution

to the already existing literature on the subject. While laying no claim to completeness, the author nevertheless has succeeded in bringing together a great deal of information about this difficult and confusing group and has arranged it in such a way that the work still remaining to be done, in order to have a complete record of this sub-family, will be apparent to those workers who are especially interested in filling in the gaps. His main object was to "describe and figure all of the known American species in such a way that they can be readily recognized in as many stages as possible." For every species ever reported in America he describes one stage and usually two or three. A chapter on the general morphology and one on the biology of the Adelginae precedes the taxonomic treatment.

There is a bibliography of 161 titles and an index. The work is abundantly and well illustrated.

WILD ANIMAL INTERVIEWS *and Wild Opinions of Us.*
By William T. Hornaday.
Charles Scribner's Sons
$2.50 5¾ x 8; xiv + 310 *New York*

A jolly book, in which much accurate information concerning the natural history of wild animals is scattered amongst a quantity of imaginary argumentation, discussion, and badinage between all kinds of animals and the interviewer. We commend to the attention of the cautious laboratory boys Hornaday's forthright remarks about animal psychology. They are scientifically indefensible, but not therefore necessarily or wholly false.

> Any naturalist who is worth his salt can determine the thoughts and feelings of mammals, birds, and reptiles by the sign language, by facial and bodily expression, and by telepathy; and afterward he can easily translate the whole interview product into outdoor English for the benefit of the reading classes. . . . . Neither the youngsters nor the oldsters of to-day are fully aware of the breadth and depth of the wild animal mind, the wonderful scope of its reasoning, or the high quality of its conclusions.

This book should be very popular with young folks from about eight to twelve years and especially with those who in their earlier years enjoyed the Peter Rabbit Series.

THE BIOLOGY OF SPIDERS.
By Theodore H. Savory. The Macmillan Co.
$5.50 5⅜ x 8½; xx + 376 *New York*

This compendium of material collected from many sources, including also much of the author's original work, is a sound and much needed treatise on the natural history of the arachnids. It contains much that is of interest to the general reader as well. Some idea of its scope is indicated in the chapter headings: The external structure of spiders; the internal structure of spiders; the senses and sense organs; the behaviour of spiders; the quest for food; the spider's web; the spider and its environment; the distribution of spiders; the courtship of spiders; the mating and parenthood of spiders; the development of spiders; fossil and primitive spiders; the trap-door spiders; the evolution of spiders; some other arachnida.

The numerous illustrations are well chosen. There is a lengthy bibliography and an index.

DESTRUCTIVE AND USEFUL INSECTS.
Their Habits and Control.
By C. L. Metcalf and W. P. Flint.
McGraw-Hill Book Co., Inc.
$7.50 5¾ x 9; xii + 918 *New York*

A general textbook of entomology,

developed on an economic base. The first ten chapters deal with general topics, morphology, physiology, classification and control. The remainder of the book is devoted to the discussion of the insects injurious to various crops, domestic animals and man. It is extensively illustrated, but mostly with borrowed figures, and indexed in great detail. It should serve a useful purpose, particularly in agricultural colleges.

COMMON BIRDS OF NORTH CAROLINA GARDENS, FARMS AND ORCHARDS. *Extension Circular No. 170.* *By Laurence H. Snyder.*

N. C. Agricultural Extension Service

10 cents 6 x 9; 47 (paper) *Raleigh*

This bulletin is presented to meet the demand for a small booklet giving the names and descriptions of common birds of North Carolina. The subject matter is based on observation made over many years in that State. In addition free use has been made of Pearson and Brimley's *Birds of North Carolina*, and various publications of the U. S. Department of Agriculture. The pictures were drawn from actual specimens. The list of birds described includes only 100 of the commonest forms.

A DISTRIBUTIONAL SUMMATION OF THE ORNITHOLOGY OF LOWER CALIFORNIA. *University of California Publications in Zoology, Vol. 32, No. 1.* *By Joseph Grinnell.*

University of California Press

$3.75 7 x 10¾; 300 (paper) *Berkeley*

This survey was undertaken to find out just what birds exist within the territory of Lower California, together with the outstanding facts as to the local and seasonal occurrences of each of the species and races. Although the task proved to be far more laborious than had been anticipated, the author has succeeded in setting a standard for future work in western ornithology. There is a bibliography of 461 titles and an index to scientific and vernacular names.

LEHRBUCH DER PROTOZOENKUNDE. *Eine Darstellung der Naturgeschichte der Protozoen mit Besonderer Berücksichtigung der Parasitischen und Pathogenen Formen. Fünfte Auflage. II. Teil, Spezielle Naturgeschichte der Protozoen. Erste Hälfte: Mastigophoren und Rhizopoden.* *Edited by Franz Doflein and Eduard Reichenow.* *Gustav Fischer*

22 marks 6¾ x 10⅛; 426 (paper) *Jena*

The first part of this new edition of the Doflein textbook of protozoology has already been noticed in these columns (III, 586). The present part is the first half of the special portion of the whole work. It deals with Mastigophora and Rhizopoda. It is beautifully printed and illustrated, and constitutes a solid addition to the reference literature of zoology.

DIE TIERWELT DER NORD- UND OSTSEE. *Lieferungen XII und XIII.* *Edited by G. Grimpe and E. Wagler.*

Akademische Verlagsgesellschaft m.b.H. Leipzig

Lief. XII, 20.25 marks 6 x 8½; 238 (paper)
Lief. XIII, 13.20 marks 150 (paper)

These two parts of this useful coöperative treatise on the zoology of the North and Baltic seas, of which earlier parts have been noted in these columns, deal

with fishery biology (Schnakenbeck); Echinoderma (Mortensen and Lieberkind); Teleostei Physoclisti 7–9 (Duncker and Mohr); zoological and fishery stations (Redeke); Amoebozoa et Reticulosa (Rhumbler); Hydrozoa (Brock).

TESTS OF BLOWFLY BAITS AND REPELLENTS DURING 1926. *U. S. Department of Agriculture Technical Bulletin No. 80.*
By D. C. Parman, E. W. Laake, F. C. Bishopp and R. C. Roark.
U. S. Government Printing Office
5 cents $5\frac{3}{4}$ x 9; 14 (paper) *Washington*

The chief results of this study are the following:

Beef liver, hog liver, and rabbit meat are all attractive to blowflies and are suitable for bait. The age of the meat, and whether it is in chunks or ground, affect its attractiveness to flies, and apparently chilling also has some influence.

The type of container affects the attractiveness of the bait to flies. A transparent container is more attractive than an opaque one.

The most promising blowfly repellents found as the result of this investigation are pine-tar oil (now being used on an extensive scale by ranchmen), pyrethrum, and certain copper compounds.

AN OUTBREAK OF HOUSE MICE IN KERN COUNTY, CALIFORNIA. *University of California Publications in Zoology, Vol. 30, No. 7.*
By E. Raymond Hall.
University of California Press
25 cents $7\frac{1}{4}$ x $10\frac{3}{4}$; 14 (paper) *Berkeley*

This paper furnishes an excellent illustration of what unfortunate results man sometimes unwittingly produces when he attempts to reduce the numbers of certain kinds of animals in a particular region. In this instance, under favorable meteorological conditions, when food and shelter were abundant and the principal natural enemies of house mice that normally held their numbers in check had been removed, literally millions of them laid waste a region 18 miles in diameter.

BOTANY

THE FERNS (FILICALES). *Treated Comparatively with a View to Their Natural Classification. Volume III. The Leptosporangiate Ferns.*
By F. O. Bower. Cambridge University Press
30 shillings net *Cambridge*
7 x $10\frac{1}{4}$; viii + 306

This is the concluding volume of Professor Bower's work on the phylogeny of the ferns. He here considers the leptosporangiate ferns, having discussed in the first volume the general methods of phyletic study, and in the second volume applied these methods to the study of the primitive ferns, especially the Eusporangiatae.

The author regards his conclusions with proper reserve; in his own words:

In a sense then this work may be held as opening a fresh period in the Classification of Ferns. It is the sincere hope of the author that it may stimulate further enquiry, suggest the use of still other criteria of comparison, and perhaps lead finally to other conclusions than those here adopted.

His final chapter deals with the evolutionary bearing of his work and will be of interest to biologists generally. He holds that while experiment may give illuminating results, it cannot safely be held to reconstruct evolutionary history, and that comparative morphology, checked by palaeontology, must remain the foundation for phyletic conclusions. As applied to the ferns, we find clear evidence that the main phyla, though distinct at least from early Mesozoic time,

have still developed in similar directions. The author holds that the evidence indicates that the so-called fluctuating variations, whose hereditary nature orthodox Mendelians deny, may, if continued without time-limit, become hereditary. Probably no hard-boiled Mendelian will agree, and we confess that his arguments are obviously not conclusive; but for that matter all the other arguments for other theories of evolution that have come to our attention seem to us equally inconclusive, and there you are.

BACTERIOLOGY. *A Text-book of Micro-organisms.*
By Fred W. Tanner. John Wiley and Sons, Inc.
$4.50 5¾ x 9; xvii + 548 *New York*

PRACTICAL BACTERIOLOGY. *An Introduction to Bacteriological Technic.*
By Fred W. Tanner. John Wiley and Sons, Inc.
$2.50 5¾ x 9⅛; xiv + 235 *New York*

This introductory text devotes a generous portion of its space to presenting in summary fashion collateral information in biology, chemistry and physics as well as to practical applications. The style is undistinguished.

The laboratory guide for students who are beginning the study of bacteriology was prepared to accompany the author's own text book but is so arranged that it can be used with other texts.

THE MOTOR MECHANISM OF PLANTS.
By Sir Jagadis Chunder Bose.
Longmans, Green and Co.
$8.40 5½ x 8⅝; xxv + 429 *New York*

This enthusiastic advocate of the identity of the physiological responses of plants and animals has collected in book form all of his results pertaining to the motor mechanism of plants. Many of these have previously appeared in print. There are treated here not only the visible external movements of plants but also the invisible internal movements concerned with propulsion of sap. Single and multiple responses and automatic movements are described and their functional importance in the life of the plant discussed. Throughout the book the motor mechanisms of plants and animals are compared and contrasted. There is nothing in this volume which makes the author's well-known position any more likely to be accepted by plant physiologists than it was before.

DIE HÖHEREN PILZE. *Basidiomycetes. Mit Ausschluss der Brand- und Rostpilze. By Gustav Lindau (Third edition, entirely rewritten by Eberhard Ulbrich).*
Julius Springer
29.50 marks *Berlin*
5½ x 8⅛; xii + 497 + 14 plates

The third edition of a standard German handbook for the identification of mushrooms. It has been extensively revised from the second edition by Professor Ulbrich. Most of the illustrations have been segregated from the text and printed separately in a pamphlet, which is tucked in a pocket on the inside back cover of the book. A useful book.

WASSERPFLANZEN UND SUMPFGEWÄCHSE IN DEUTSCH-OSTAFRIKA.
By A. Peter. *Weidmannsche Buchhandlung*
20 marks *Berlin*
6½ x 10; 129 + 19 plates (paper)

A taxonomic treatise, with an ecological viewpoint.

MORPHOLOGY

THE FROG. *An Introduction to Anatomy, Histology, and Embryology.*
By A. Milnes Marshall (edited by H. G. Newth). *The Macmillan Co.*
$2.00 $4\frac{1}{2}$ x $7\frac{1}{8}$; x + 182 *New York*

Owing to the death in 1926 of Professor F. W. Gamble, who for many years edited this laboratory classic, H. G. Newth, Lecturer in Zoology at the University of Birmingham, has inherited the task of preparing the 12th edition. In general, the book remains the same, except for the sections dealing with microscopical technique, which have been brought up to date, and those dealing with the germ-cells and the early stages of development, which have been largely re-written.

DEGENERATION AND REGENERATION OF THE NERVOUS SYSTEM. *Volumes I and II.*
By S. Ramon y Cajal. Translated and Edited by Raoul M. May. *Oxford University Press*
$18 for 2 vols. *New York*
6 x $9\frac{1}{8}$; xxviii + 769

This treatise by the renowned Nobel laureate of Spain is an exhaustive consideration of what is known concerning the "regressive and progressive processes in the nervous fibres and cells, of traumatic origin, and especially of those due to expansional mutilation." It is a classic work.

ATLAS OF HUMAN ANATOMY. *Vol. I. The Bones, Ligaments, Joints, Regions and Muscles of the Human Body. Vol. II. The Viscera Including the Heart. Vol. III. The Nervous and Blood Vascular Systems and the Sense Organs of the Human Body, with an Appendix on the Lymphatic System. By Johannes Sobotta (Edited from the sixth German edition by J. Playfair McMurrich).*
G. E. Stechert and Co.
$15.00 $7\frac{5}{8}$ x $9\frac{5}{8}$; xxiv + 785 *New York*

Edited and translated from the sixth German edition. It excludes much of the textual matter contained in former editions and conforms more strictly to the title of an anatomical atlas. It continues to vie with Spalteholz for supremacy as the standard reference atlas. The choice between the two is a matter of the toss of a coin.

PHYSIOLOGY AND PATHOLOGY

A HISTORY OF PATHOLOGY.
By Esmond R. Long.
The Williams & Wilkins Co.
$5.00 5 x $7\frac{1}{4}$; xxiv + 291 *Baltimore*

This general survey of the steps by which the study of pathology has reached its present form was prepared primarily for the author's own students in the University of Chicago, where he is Professor of Pathology. It will be of much interest, however, to all biologists who are interested in following through the development and growth of this phase of their subject.

The idea of humoral pathology in vogue in the time of Hippocrates was upheld by Galen, whose influence extended for a thousand years or so and was in the main supreme down to the renaissance. It was not until the 15th century that the precedent of performing necropsies was established. Fernel, while still holding to the older teachings as regards the pathological effects of humors, temperaments and vital spirits, developed a more rational general pathology than his predecessors. It was

Harvey's great discovery that had a more far reaching effect in pathology than probably any other single discovery. From this time on rapid strides were made.

Modern pathology properly begins with Morgagni, his case histories, numbering several hundreds, being masterly descriptions. With the discovery of the cell, Virchow rebuilt the science of pathology and again it received fresh impetus. New discoveries followed in rapid succession. The last chapters of the book deal with pathological histology, the rise of bacteriology and immunology, and experimental and chemical pathology. The author suggests that future progress in pathology will not be made by individuals so much as by organizations for research to fill in gaps in existing knowledge. There are numerous illustrations that add to the interest of the text. Col. F. H. Garrison of the Army Medical Museum has written a foreword.

THE FOOD OF JAPAN. *Publications of the League of Nations. III. Health. 1928. III. 2.*

By Egerton C. Grey. *World Peace Foundation*

$1.25 6¼ x 9½; 161 (paper) *Boston*

Statistical and analytical data to supply information which can be used as a basis for an investigation of the relation of food to the health of the people. The work was undertaken in behalf of the Health Section of the League of Nations and was carried out in the Imperial Institute of Nutrition, Tokyo. The first two chapters deal with the quantity and quality of food in Japan, chapter III with the distribution of food and chapters IV and V with the chemical composition of Japanese foods as consumed, and as purchased. Numerous tables exhibit the statistical and analytical data. There is an appendix giving the Japanese literature relating to the chemical and physical properties of the food of the Japanese, and another containing lists of food materials and the plants and animals serving as sources of food in Japan. These latter lists are in Latin, Japanese and English.

LECTURES ON PLANT PATHOLOGY AND PHYSIOLOGY IN RELATION TO MAN. *A Series of Lectures Given at the Mayo Foundation and the Universities of Minnesota, Iowa, Wisconsin, the Des Moines Academy of Medicine, Iowa, and Iowa State College, 1926–1927.*

W. B. Saunders Co.

$2.50 5 x 7¾; 207 *Philadelphia*

These are a group of lectures given by different workers at different institutions on topics related to plant diseases and their importance for man, and collected by the Mayo Foundation. They vary in length as well as the emphasis given to points of general or special interest, but for the most part stress the practical importance of the subjects considered. They are: Filterable Viruses, by L. O. Kunkel; Ecology and Human Affairs, by H. C. Cowles; Some Aspects of the Fusarium Problem, by G. H. Coons; Racial Specialization in Plant Disease Fungi, by E. C. Stakman; The Relation of Plant Pathology to Human Affairs, by H. H. Whetzel; and Some Aspects of Cellular Physiology, by W. J. V. Osterhout.

A bibliography is provided with each chapter and there is a general index appended to the book.

NEUE WEGE ZUR WASSERSTERILISIERUNG (KATADYN).

By Georg A. Krause. *J. F. Bergmann*

1.20 marks 6 x 9⅜; 20 (paper) *München*

The author claims to have developed a new method by means of which water may be rendered sterile with greater efficiency than attained by any method used hitherto. It is based on the discovery that water which has been in contact with metals such as copper or mercury takes on oligodynamic properties and becomes bactericidal. Silver may be rendered specially effective for the purpose by subjecting it to an inflating process, and it is then called "katadyne" silver. By use of the method the author, according to his experiments, has been exceedingly successful in rendering water sterile of a variety of bacterial forms.

HOMOIOTHERMISM. *The Origin of Warm-Blooded Vertebrates.*
By A. S. Pearse and F. G. Hall.
John Wiley and Sons, Inc.
$2.00 5⅜ x 8⅝; ix + 119 *New York*

This book is concerned with the physiological and ecological aspects of the evolution of poikilothermic into homoiothermic animals. In it we attempt to discuss evidence for the origin of homoiotherms, temperature regulation, the factors influencing rate of metabolism and growth, and other matters which relate to the adjustments associated with evolution from erratic, more or less intermittent, living to uniform, constant living.

The promise of a fascinating and important study implied in this introductory statement is only partially fulfilled in the body of the book. The whole work is rather brief, and is taken up largely with a review of the elementary facts of metabolism, the specific questions of homoiothermism and poikilothermism being brought in only collaterally. Withal it is an interesting short consideration of the general question of body temperature. There is a bibliography and an index.

SYPHILIS. *Acquired and Heredosyphilis.*
By Charles C. Dennie. *Harper and Bros.*
$2.50 4¼ x 6¾; xiii + 304 *New York*

This volume initiates a series of medical monographs the scope and purpose of which are indicated by the editor as follows:

They will be monographs in the sense that each volume will be devoted to but one subject, but it is not designed that they will be complete in every respect. Rather will they be practical, presenting the essential features of the subject in such form as to make them easily available. They will be written with the needs of the general practitioner particularly in mind by men whose large consulting practices have given them broad contact with the family physician and who are therefore familiar with his requirements.

The book is extreme in its summarization and if useful at all only as a "handbook." At least some of the judgments expressed without supporting evidence are dubious. It contains neither bibliography nor index.

STUDIES ON SCURVY. *Stanford University Publications. Medical Sciences Vol. II, No. 2.*
By Arthur W. Meyer and Lewis M. McCormick. *Stanford University Press*
$2.25 *Stanford University*
7 x 10; 107 (paper)

The first two parts of this monograph are by Arthur W. Meyer and deal with the symptomatology and the gross and minute morphology of experimental scurvy in the guinea pig. The last section, on some characteristics of the blood of the guinea pig in experimental scurvy, is by Lewis M. McCormick. A list of references is appended to each part. There are a number of excellent photographic plates.

LECTURES ON CONDITIONED REFLEXES. *Twenty-five Years of Objective Study of the Higher Nervous Activity (Behaviour) of Animals.*
By Ivan P. Pavlov (Translated from the Russian by W. Horsley Gantt, with the collaboration of G. Volborth, and an Introduction by Walter B. Cannon).
International Publishers
$6.50 6 x 9¼; 414 *New York*

A translation of forty-one papers by Pavlov, dating from 1903 to 1928. There is also a biographical sketch by the translator. For the reader who desires a consecutive account of Pavlov's work, and of the general theory of the conditional reflex, this book will probably be less satisfactory than Pavlov's volume on Conditioned Reflexes reviewed here March, 1928. For the reader who wishes to trace the development of Pavlov's thought, however, the present volume will be invaluable.

ANNALS OF THE PICKETT-THOMSON RESEARCH LABORATORY. *Vol. IV. Part I. The Pathogenic Streptococci. An Historical Survey of Their Rôle in Human and Animal Disease.*
$10 per volume (Parts I and II)
The Williams & Wilkins Co.
Part I *Baltimore*
8½ x 11; vii + 250 (paper)

The present volume of these Annals is devoted to a historical survey of researches on the relations of the *Streptococci* to disease; the diseases considered in this part are rheumatic fever, chorea, erythema nodosum, and carditis. The concluding part of this volume is to consider acute suppurative arthritis, chronic arthritis, oral and dental sepsis, and tonsillitis.

FINAL REPORT OF THE LEAGUE OF NATIONS INTERNATIONAL COMMISSION ON HUMAN TRYPANOSOMIASIS. *Publications of the League of Nations. III. Health. 1927. III. 13.*
World Peace Foundation
$5.00 7¾ x 10; 392 (paper) *Boston*

Contains the following: Report of the new sleeping-sickness focus at Ikoma, by F. K. Kleine; Studies on the bionomics of the polymorphic trypanosomes of man and ruminants, by H. Lyndhurst Duke; Reports, by G. Lavier; Reports, by M. M. Prates; Pathologico-anatomical and serological observations on the trypanosomiases, by M. Peruzzi; Epidemiology of sleeping-sickness in the *G. palpalis* and *T. gambiense* areas and various observations on treatment; General recommendations for the control of sleeping-sickness in African dependencies, by F. K. Kleine, L. Van Hoof and H. Lyndhurst Duke.

THE RETINAL CIRCULATION *in the Normal and Pathological State.*
By P. Bailliart (Translated by James E. Lebensohn). *The Professional Press, Inc.*
$3.50 5 x 7½; 220 *Chicago*

A useful little treatise for the medical man who uses the ophthalmoscope daily for diagnostic purposes. The first four chapters describe the anatomy and physiology of the retinal circulation. The next four deal with functional disorders of the circulation. The remainder of the book is devoted to the discussion of lesions of the retinal vessels and their appearance in different diseases. There is no index.

AN ESSAY ON HASHEESH. *Historical and Experimental. Second Edition.*

By Victor Robinson. *Medical Life Press*
$1.00 5 x 7½; 91 *New York*

A reprint of an entertaining little study of *Cannabis indica*. The author has given a useful account of the preparation and uses of the drug; but the most interesting part of the book to most people will undoubtedly be his account of his experiments with hasheesh, both on his friends and on himself.

THE NORMAL AND PATHOLOGICAL PHYSIOLOGY OF BONE. *Its Problems. By R. Leriche and A. Policard. English translation by Sherwood Moore and J. Albert Key.* *The C. V. Mosby Co.*
$5.00 6 x 9; 236 *St. Louis*

This is in the nature of a personal memoir giving the opinions of the authors concerning the processes of bone formation and destruction based on a long interest in the subject and extensive study. It is written with a strong physico-chemical bias, not supported in the text with detailed facts. The generalizations indulged in appear to run beyond the evidence given. It is graced by originality and courage, however, and is a stimulating consideration of the basic problems of bone physiology. There is an exhaustive bibliography and an index.

CANCER. *Its Cause and How to Prevent It. With an Epilogue: How to Cure Cancer (A New Theory).*
By Herman J. De Wolff.
Herman J. De Wolff
Rijswijkscheweg 55, The Hague
5½ x 8½; 19 (paper)

The author states in brief paragraphs his belief that cancer is caused by substances with tanning qualities, such as coal-tar products and many chemical substances. There is no attempt at definite proof, neither so far as the cause of cancer is concerned nor for the cure which he suggests. His treatise appears to be a curious jumble of possible truths and quackery.

THE PRESSURE PULSES IN THE CARDIOVASCULAR SYSTEM.
By Carl J. Wiggers. *Longmans, Green and Co.*
$5.00 5¾ x 8¾; xi + 200 *New York*

This volume in the series of Monographs on Physiology measures up fully to the high standard set by the initial editor, the late Ernest Starling. It is a comprehensive and authoritative summary by one of the chief contributors to the subject, of the methods of recording, and the physiological significance of pressure pulses in the cardiovascular system. There is an extensive bibliography and an index.

THE ELEMENTS OF THE SCIENCE OF NUTRITION.
By Graham Lusk. *W. B. Saunders Co.*
$7.00 net 5¾ x 9⅛; 844 *Philadelphia*

This revision, the author threatens, is the last which will be made of his noted text. It brings up to date a statement of all the scientifically established facts that relate to man considered as a fuel consuming machine.

BIOCHEMISTRY

ORGANIC LABORATORY METHODS. *By Professor Lassar-Cohn. Authorized translation from the general part of fifth revised*

edition by Ralph E. Oesper. Edited by Roger Adams and Hans T. Clarke.

The Williams & Wilkins Co.

$6.50 6 x 9; xi + 469 *Baltimore*

This book is a translation of the first volume of the fifth revised German edition. It deals with general operations of laboratory technique such as distillation, crystallization, molecular weight determinations, sublimation, etc. Dr. Lassar-Cohn, who died in 1922, before the fifth edition appeared in print, made no claim for completeness in his work. In such an extensive field, where new methods are so constantly appearing, it would have been impossible to make it all inclusive. Neither did he conceive it to be a text book for beginners. Rather it was "to cite and outline the methods by which typical difficulties have been overcome and leave the adaptation of the suggestions to the problem at hand to the resourcefulness of the reader." This manner of presenting the subject of organic chemistry makes the book a most valuable one to have at hand in the laboratory.

THE COLLOID CHEMISTRY OF PROTOPLASM.

By L. V. Heilbrunn. *Gebrüder Borntraeger*

19 marks (paper) *Berlin*

21 marks (cloth)

6 x 9; viii + 356

This excellent book, written while the author was a visitor in various European laboratories, critically summarizes recent work in the field of the colloid chemistry of protoplasm. After the introductory chapters, there follow sections on methods of study; the absolute viscosity of protoplasm; the elasticity of protoplasm; the action of temperature, of various salts, of acids and alkalies and of fat solvents upon viscosity; the surface precipitation reactions; a specific colloid chemical reaction peculiar to living organisms; cell division; and protoplasmic activity.

CHEMISTRY IN MEDICINE. *A Co-operative Treatise Intended to Give Examples of Progress Made in Medicine with the Aid of Chemistry.*

Edited by Julius Stieglitz. Advisory Editors: Anton J. Carlson, Reid Hunt, Frank R. Lillie, Lafayette B. Mendel, H. Gideon Wells.

The Chemical Foundation, Inc.

$2.00 5¼ x 7½; xxi + 757 *New York*

The Chemical Foundation, through its president, F. P. Garvan, issued this book, without profit, to the public to further an appreciation of the contributions of chemistry to medicine. An able group of contributors has been gathered by the editor to present various aspects of the subject. The following are the general topics discussed: The significance of chemistry and of its methods of attack on fundamental problems; heredity and development; the human body as a machine; the story of the discovery of the vitamins; the conquest of dietary diseases; chemical regulators of the body; the policing of civic life in the laboratory; the alleviation of suffering; the war on invading germs; a hope of mankind—chemotherapy. A glossary of technical terms and an index are appended.

DIE METHODIK DER FERMENTE. *Lieferungen IV und V.*

Edited by Carl Oppenheimer and Ludwig Pincussen. *Georg Thieme*

28 marks each *Leipzig*

IV: 7⅝ x 10⅝; xxx + 314 (paper)

V: vii + 320 (paper)

The parts of this encyclopedic work on ferments previously issued have been noted in this REVIEW (Vol. III, No. 3; Vol. IV, No. 1). The present issue

completes the work and comprises the following:

Part IV, continues Division II, completing subdivision D and presenting E on proteases and F on desmolases.

Part V gives a table of contents for the entire work, continues subdivision F from Part IV, and presents G on fibrin ferments. Division III follows with subdivision A devoted to ferments in biological investigations, and B on clinical applications. A general subject index is appended.

COLLOID CHEMISTRY. *Theoretical and Applied. Vol. I. Theory and Methods. Vol. II. Biology and Medicine.*
By Selected International Contributors. Collected and Edited by Jerome Alexander.
The Chemical Catalog Co., Inc.
Vol. I, $14.50 *New York*
Vol. II, $15.50
6 x 9; 974 (Vol. I)
1029 (Vol. II)

This extremely useful reference work should be in every biological laboratory. There are over 100 chapters, contributed by nearly as many different authors, on various aspects of the physics and chemistry of colloids. Naturally the treatment is uneven. It is bound to be in such a composite. But the work is a veritable mine of information, and will serve as a reference source. Abundant documentation makes it possible to go deeper into the subject where desirable.

LE pH EN BIOLOGIE.
By Marcel Verain and Jean Chaumette.
Masson et Cie
16 francs *Paris*
$5\frac{3}{8}$ x $7\frac{3}{4}$; viii + 160 (paper)

A short account of the theory and technique of hydrogen ion measurements, with some of the applications of such measurements in medicine, industry, and agriculture.

DONNÉES NUMÉRIQUES DE BIOLOGIE ET DE PHYSIOLOGIE ET CHIMIE VÉGÉTALES. *Extrait du Vol. VI des Tables Annuelles de Constantes (1923–1924).*
By E. F. Terroine and H. Colin.
Gauthier-Villars et Cie
60 francs (cloth) *Paris*
44 francs (board)
$8\frac{1}{2}$ x $10\frac{3}{4}$; viii + 88

Miscellaneous biological constants taken from determinations published in various journals during 1923–4. It supplements a similar compilation for 1910–1922 which is obtainable in a single volume.

PRAKTIKUM DER HISTOCHEMIE.
By Gustav Klein. *Julius Springer*
4.50 marks *Berlin*
$6\frac{1}{2}$ x $9\frac{3}{4}$; v + 71 (paper)

An introductory manual on microchemical methods covering inorganic, organic and animal histochemistry. There is a bibliography.

SEX

MOTHERHOOD IN BONDAGE.
By Margaret Sanger. *Brentano's*
$3.00 $5\frac{1}{2}$ x 8; xix + 446 *New York*

A collection of appeals for information on birth control, with harrowing details. They have been somewhat loosely classi-

fied, but in general they tell the same story over and over. The letters are rather more persuasive arguments for the dissemination of birth control information than the introductory and concluding passages of the book.

STATUS OF SEX EDUCATION IN THE SENIOR HIGH SCHOOLS OF THE UNITED STATES IN 1927. *A Survey under the Direction of the Surgeon General, United States Public Health Service in Collaboration with the United States Bureau of Education. V. D. Bulletin No. 87.*
By Lida J. Usilton and Newell W. Edson. *U. S. Government Printing Office*
5 cents *Washington*
$5\frac{3}{4}$ x $9\frac{1}{8}$; iv + 15 (paper)

A report of a survey made in 1927 under the direction of the Surgeon General of the United States Public Health Service, in collaboration with the United States Bureau of Education. The questionnaire method was employed. It is estimated that the percentage of all high schools giving "integrated sex education" was 8 in 1920 and 10 in 1927.

BIOMETRY

THEORY OF PROBABILITY.
By William Burnside. *The Macmillan Co.*
$3.50 $5\frac{1}{2}$ x $8\frac{5}{8}$; xxx + 106 *New York*

These essays on probability by the late William Burnside were collected into this single volume after his death. They comprise a manuscript which he had almost completed for publication, and are issued without change as the author left them. There is a formal treatment of the elementary notions of probability that brings out again the unsatisfactory basis of the subject from a mathematical viewpoint, and in successive chapters a consideration of some of the classical variety of problems progressively arranged to lead into the Gaussian Law of Errors. A certain amount of obscurity is added to the essential difficulty of the subject by the use of a notation not everywhere explicitly defined.

There is an introductory essay on the life of the author by A. R. Forsythe and appended to the book is a list of cognate papers by him. Considering the small amount of literature in English by original writers on the subject of mathematical probability the publication of this volume by the Cambridge University Press is to be commended.

KORRELATIONSRECHNUNG.
By Franz Baur. *B. G. Teubner*
1.20 marks *Leipzig*
$4\frac{3}{4}$ x $7\frac{1}{4}$; vi + 57 (paper)

This booklet gives a brief statement of the formulae of elementary probability leading into the correlation coefficient and correlation ratio. The viewpoint is that of A. A. Tschuprow's *Grundbegriffe und Grundprobleme der Korrelationstheorie*, and for adequate treatment that work had best be consulted.

STATISTIK.
By H. Moeller. *Spaeth und Linde*
8.20 marks *Berlin*
$6\frac{3}{4}$ x $10\frac{1}{8}$; xiv + 149

An elementary textbook of general statistics, with emphasis rather more heavily laid upon commercial and economic statistics than upon other departments. The brief bibliographies are confined almost exclusively to German literature.

PSYCHOLOGY AND BEHAVIOR

COMMON PRINCIPLES IN PSYCHOLOGY AND PHYSIOLOGY.
By John T. Maccurdy. *The Macmillan Co.*
$6.00 6¼ x 9⅜; xvii + 284 *New York*

This is an important book. It develops concretely Whitehead's purely philosophical idea of "pattern" and carries it to something approaching the bitter logical end in respect of biological matters falling in the general fields of brain physiology and psychology. Unfortunately it is so written as to be rather heavy reading, and on that account will doubtless fail in some degree to get the immediate attention from biologists which it deserves. From the viewpoint of psychology the author's position is in close resemblance at least to that of the adherents to the *Gestalt* theory. From the point of view of biology its chief significance is in its demonstration that an extreme mechanistic position is untenable.

HOWS AND WHYS OF HUMAN BEHAVIOR.
By George A. Dorsey. *Harper and Bros.*
$3.50 5½ x 8; vii + 298 *New York*

Following the publication of *Why We Behave Like Human Beings* the author received something over 12,000 letters about it all. This present book is written for the purpose of answering some of the questions raised in these letters. Like everything that Dr. Dorsey writes it is entertaining, if somehow rather hectic and breathless reading. He is still very much of a Watsonian behaviorist. In fact the whole book is essentially just a continuation and further elaboration of the earlier one. To many academic biologists, perhaps most, the style and philosophy of these books is offensive. But after all perhaps it is better for stenographers and soda fountain clerks to get a little sound knowledge of biology by this route, than for them to get none at all, which is the net contribution of the *Professoren* to their intellectual cravings. As Mr. Coolidge so wisely said, it takes all kinds of people to make a world.

LE TRAUMATISME DE LA NAISSANCE. *Influence de la Vie Pré-Natale sur l'Évolution de la Vie Psychique Individuelle et Collective.*
By Otto Rank. *Payot*
20 francs 5½ x 9; 256 (paper) *Paris*

In recent years both obstetricians and psychiatrists have been paying a good deal of attention to the remote psychological consequences of the biologically difficult journey along a too narrow pathway which every human being is compelled to undertake if and when he enters this vale of tears. In this volume a psychoanalyst says his say about this important matter. It makes interesting reading whether you believe it or not. Who would have thought, for example, that the explanation of homosexuality is, *tout simplement*, that it is merely the result of an aversion to the female genital organs resting upon the rough experience had with them in being born? We recommend this volume to all students of human biology. They will find many ideas of interest in it, even though they are not prepared to go the whole psychoanalytic hog.

PROBLEMS OF INSTINCT AND INTELLIGENCE.
By Major R. W. G. Hingston.
The Macmillan Co.
$3.25 5⅜ x 8; vii + 296 *New York*

An extremely interesting and valuable contribution on the literature of compara-

tive psychology. The author is a distinguished naturalist and presents, in large part, the results of his own observations and experiments on insects in the field; chiefly in the jungles of the Oriental tropics. His final conclusion is that:

> So far as I can judge from the evidence given, we are not justified in making barriers between insect and human mentality. I mean we have no right to regard their minds as being totally different in kind. In their main essential characteristics the minds of these humble creatures operate in the same way as the mind of man.

THE ART OF THINKING.
By Ernest Dimnet. *Simon and Schuster*
$2.50 $4\frac{5}{8}$ x $7\frac{3}{4}$; xii + 216 *New York*

This urbane and gossipy essay on the pleasures of the intellectual life furnishes entertaining reading, and the advice it gives is sound. The book is said to have been written for "average minds." Its accuracy of aim is, then, excellent, for it has been for some months a "best seller." The thing which most amuses us in reading it is the thought it conjures up of the heavy weather that earnest thinkers in women's clubs throughout the land are going to have in trying to put the good Abbé Dimnet's precepts into practice. The poor dears will sweat; and, alas, to no purpose, we greatly fear.

THE INFERIORITY FEELING.
By William S. Walsh.
E. P. Dutton and Co., Inc.
$2.50 5 x $7\frac{3}{8}$; xi + 381 *New York*

A popular book on the inferiority complex or "feeling" as the author wisely prefers to call it. It is a temperate discussion, with sound advice for the afflicted. It is a book which all parents might well read, because most of our adult mental ills appear to have their foundations laid in early childhood. There is a brief, but well chosen bibliography.

THE FUTURE OF AN ILLUSION.
By Sigmund Freud. Translated by W. D. Robson-Scott.
Horace Liveright and the Institute of Psychoanalysis (Boni and Liveright)
$2.00 $5\frac{3}{4}$ x $8\frac{7}{8}$; 98 *New York*

Dr. Freud tells us what religion is and what is to happen to it. So far as the book has any merit, it seems to us to have acquired it by borrowing; those parts whose derivation we do not recognize, and which we accordingly credit to Dr. Freud, seem to us the questionable parts of the argument.

STUDIE ÜBER MINDERWERTIGKEIT VON ORGANEN.
By Alfred Adler. *J. F. Bergmann*
4.20 marks *München*
$6\frac{1}{2}$ x $9\frac{3}{4}$; 92 (paper)

A reissue of Adler's well-known classic on organ inferiority and its psychological consequences, which was first published in 1907 and has long been out of print.

DE OMNIBUS REBUS ET QUIBUSDEM ALIIS

FROM MAGIC TO SCIENCE. *Essays on the Scientific Twilight.*
By Charles Singer. *Boni and Liveright*
$7.50 $6\frac{1}{4}$ x $9\frac{3}{4}$; xix + 253 *New York*

In this extraordinarily interesting book, the distinguished author treats of that era in European civilization when there was a slow decline from the intellectual effi-

ciency of classical antiquity down to the lowest stages of decomposition of science, theology, and literature. After lying becalmed in the slough of magic for centuries, observational science slowly and by scarcely perceptible stages reasserted itself. Only the earliest and first steps of this recovery, are treated here. There is little concerning the development of science later than the 12th century, although some of the essays indicate a general line of treatment of the later periods. The main parts of all of these essays have appeared elsewhere in print, but with the exception of the first, they have been considerably modified. In the first chapter there is a discussion of the decay of the conception by the Ionian Greeks of the universe as a rational system. The second essay traces, in barest outline, the entire course of medieval science—and as such is the key to the volume. In the third, "The Lorica of Gildas the Briton" represents the most extreme magical degradation of the classical and ecclesiastical traditions. Science, theology and literature have sunk to their lowest depths. There then follows a chapter on early English magic and medicine—one on early "Herbals" and one on the visions of Hildegard of Bingen. In the final chapter, the medical school of Salerno of the 11th century, the first institution of Western Europe that in any way resembled a university, is described and the influence of Arabian culture traced.

While one can scarcely single out any one chapter as being more interesting than the others, possibly the fifth and sixth—on "The Early Herbals" and "The Vision of Hildegard of Bingen"—will be found the most fascinating by the general reader.

The volume is superbly printed and illustrated.

ODDITIES. *A Book of Unexplained Facts. By Rupert T. Gould. Frederick A. Stokes Co.* $4.00 5½ x 8½; 336 *New York*

This is one of the most entertaining books we have read in many a long day. While it deals with biological matters only in minor part, nevertheless biologists will enjoy reading it. We commend it to all and sundry.

The author is a retired naval officer, and is one of the most extensively, oddly, and casually erudite persons ever heard of. In a passing footnote he says: "Some years ago I read through both *Chambers's Encyclopaedia* and *The Encyclopaedia Britannica*. Truth compels me to state that I greatly prefer the former—not merely because it is shorter, but because, in my opinion, it is planned on far sounder lines, and with a much better sense of proportion."

In *Oddities* Lieut.-Commander Gould discusses some eleven cases of natural or mathematical phenomena, about which the facts are well attested, but for which no rational explanation has ever been found. In some cases he himself reaches what seems a probable explanation, but the others are left as practically complete mysteries.

The first chapter in the book deals with the extraordinary series of tracks found in the snow in Devonshire on February 8, 1855. There can be no question as to the existence and form of the tracks, but what kind of creature made them? The Berbalangs of Cagayan Sulu, Crosse's Acari, and The Wizard of Mauritius also discuss matters of direct biological interest. Regarding the acari all biologists will feel that they know the explanation *in general*, but even so the case presents some matters of detail which suggest interesting and probably profitable lines of research.

In any case, read the book!

BEYOND THE ELECTRON.

By J. J. Thomson. *The Macmillan Co.*
80 cents 5 x 7¼; 43 (paper) *New York*

These are trying times for the reasonable mind that sees the universe as a composite of well defined units that will yield understanding to persistent inquiry. Hitherto those who would not accept such clear-cut analysis, and labored the epistemological difficulties of such a view, could be damned with the epithet "philosophers." But nowadays it is the most hard boiled scientists who are introducing a fringe of nebulousness to the ultimate elements of knowledge. Here we find the great physicist of the Cavendish Laboratory saying

> a moving electron, even a uniformly moving one, is always accompanied by a series of waves. These waves as it were carry it along and determine the way it is to go; thus a moving electron is a much more complicated thing than a small point charge of electricity in uniform motion.

What hope is there for a simple view of nature when even the electron turns out complex, and where can we look for the good old mechanical determinism when a particle has to ask a wave, which it creates, how to move? The author takes up his subject as an experimentalist, and pursues it from the viewpoint of classical dynamics but his conclusions harmonize with those arrived at by way of the new wave mechanics of de Broglie and Schrödinger. In view of the alarming fact that the latter seem to imply a measure of uncertainty in mechanical events, this is notable. The forces of teleology are closing in on us.

THE NATURE OF THE PHYSICAL WORLD.

By A. S. Eddington. *The Macmillan Co.*
$3.75 5¾ x 8½; xvii + 361 *New York*

A brilliant exposition, in popular and witty language, of the revelations of relativity theory and modern atomic physics and their meaning for the problem of securing certain knowledge of the external world. Dr. Eddington comes out for the inadequacy of the scientific method and the sovereignty of the mystical insight into truth. His case against the perfection of science carries conviction but his espousal of mysticism does not. In science, however limited, there are objective criteria for distinguishing truth from illusion, but there is no arguing the case of the mystic. It either appeals to you or it doesn't. *De gustibus*, etc.

COSMOS LIMITED.

By Mary Keyt Isham. *Walter Neale*
$2.00 5¼ x 7¾; 125 *New York*

We take it that the author's justification for this book is contained in the following sentence:

> Imagination can never be wild enough to outrun the truth; and every behavior of every individual,—and not the least his imagination,—is impressed upon the mobile, ambient cosmos and makes its contributions to reality.

A general notion of the character of the book can be had from a few quotations.

> Time is the sensing of registration upon cell tissue of its environmental conditions. It is an old touch sense, which, as now experienced by the ear, a highly specialized organ, is the sound sense. All the cells realize impact, which is an incipient hearing and produces a pulsing cellular sensation, a general consciousness of passing time. Marking the passing of the organism through solar radiants, the time sense is occupied in light.
>
> Every cell of the body is an organized assemblage of sunpoints. When points enter the organism in various ways,—as through the respiratory tracts, the alimentary canal, the sense organs,—they become

organic cumulants. Feeling is the motion of an organic cumulant in the act of changing its condition. The abstract conception of a changing group of related points gives us the idea of a *unit of feeling*.

Space is lacking for all the passages of interest, but we cannot omit the following:

We can not escape the aesthetic demand of life. In time the mind will find a way to eliminate those disgusting bodily products, such as certain excreta which are of disagreeable odor and consistency and cause any amount of inconvenience in regard to proper care, plumbing, cleaning, and laundering. Disgust is a sign of disapproval, and when the mind appreciates its own powers, it will of its own volition finally eliminate what displeases it. This will take an indefinite number of centuries; but when it has been accomplished, solicitations and discontents on a higher plane will arise. The progressive mentality continually pushes its conflicts and urges to higher planes. The secretions and excretions will lose their present undesirable qualities, when by the proper personal selection of nutriment and by exquisitely functioning organs, food will be so readily assimilated, that waste products can be eliminated as easily as is the perspiration. But even then persons will be anxious for fear their bodies may not send forth a natural fragrance which is their favorite one. Each individual will wish to cultivate that aroma or mixture of aromas most pleasing to him. And since the body is capable of producing all the fragrances desired, the glands will be trained as personal gardens.

Even Reginald, the Office Boy, young and uninhibited as he is, cannot think of anything fitting to say about this last quotation, which is at the same time printable in a family magazine like this.

THE BON VIVANT'S COMPANION *or How to Mix Drinks.*
By Jerry Thomas (Edited, with an Introduction, by Herbert Asbury). Alfred A. Knopf $3.00 $5\frac{3}{4}$ x $8\frac{5}{8}$; li + 169 *New York*

The reason for publishing this book is thus stated by Mr. Asbury:

This volume, therefore, is an attempt to preserve for posterity a specimen of Americana which in all likelihood will never be duplicated, for it is quite improbable that there will ever again be a legitimate bartender practicing under the protection of the Stars and Stripes. The work should thus be of considerable value to the scholar who wishes to study the manners and customs of the American people in the days before drinking became extinct, and the bartender a pariah.

Professor Thomas, in the preface to the first edition, has some very sound words on the social custom of drinking, which we quote:

In all the ages of the world, and in all countries, men have indulged in "social drinks." They have always possessed themselves of some popular beverage apart from water and those of the breakfast and tea table. Whether it is judicious that mankind should continue to indulge in such things, or whether it would be wiser to abstain from all enjoyments of that character, it is not our province to decide. We leave that question to the moral philosopher. We simply contend that a relish for "social drinks" is universal; that those drinks exist in greater variety in the United States than in any other country in the world; and that he, therefore, who proposes to impart to these drinks not only the most palatable but the most wholesome characteristics of which they may be made susceptible, is a genuine public benefactor. That is exactly our object in introducing this little volume to the public. We do not propose to persuade any man to drink, for instance, a punch, or a julep, or a cocktail, who has never happened to make the acquaintance of those refreshing articles under circumstances calculated to induce more intimate relations; but we *do* propose to instruct those whose "intimate relations" in question render them somewhat fastidious, in the daintiest fashions thereunto pertaining.

The volume contains, as one might guess, formulae for the compounding of a large number of beverages now prohibited by law, including, of course, Professor Thomas's own inventions, Tom and Jerry and the Blue Blazer. Its historical value is enhanced by illustrations of typical

New York scenes of the 1870's, and also by portraits of the more illustrious bartenders of that time.

THE CORRESPONDENCE OF SPINOZA
Translated and edited, with introduction and annotations by A. Wolf.
Lincoln Mac Veagh, The Dial Press
$5.00 5½ x 8⅝; 502 *New York*

An extremely well translated, edited, and printed edition of Spinoza's letters. It is a work of first importance to every philosopher and scientific man, because it makes it easily possible to read Spinoza, instead of about him, which has been the prevailing practice. The annotations are extensive and penetrating.

THE IMPOTENCE OF MAN (*"L'Homme Impuissant"*).
By Charles Richet (Translated by Lloyd Harvey). *T. Werner Laurie, Ltd.*
7s. 6d. net 5½ x 8½; 150 *London*

The eminent investigator of ectoplasm here turns to philosophy. We regret to report that we can find no idea in the book which is not fully worked out in Epictetus or Lucretius. However, there may be some who will prefer the style of this volume; we shall stick to the classics.